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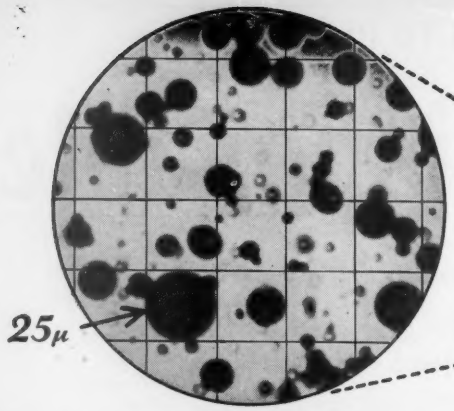

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Agricultural Engineers

The nation's professional agricultural engineering organization—the American Society of Agricultural Engineers—will celebrate a half-century of growth at its 50th annual meeting at Michigan State University, 23–26 June.

During the past decades, the efforts of these "engineers of agriculture" have been concerned with the engineering of tractors and other farm power equipment, the design of farm structures, the utilization of electric energy on farms, soil and water conservation and management, and the primary processing of agricultural products for the market.

The dispersion of agricultural production through millions of small units, instead of the intensive concentrations typical of most industries, generally obscures the scope and magnitude of the field to which agricultural engineering is applicable. The value of operating equipment on American farms is estimated at about $16 billion. Approximately 5.5 million barns and 20 million other permanent farm structures are worth something near $24 billion. The use of electric energy on American farms has increased about 1200 percent in the past 20 years, and the total annual consumption was estimated in 1955 at about 21×10^9 kilowatt hours.

American agriculture may be divided into three basic "power eras": before 1850, human power; 1850–1920, animal power; after 1920, mechanical and electric power. A direct consequence of this mechanization of our agriculture is that less than 13 percent of the population of the United States now produces all the agricultural products needed in this country (exports offset imports of commodities not grown in the United States), as compared with the 85 percent of our people required for agricultural production 100 years ago. The release of workers from American farms, accomplished largely through this mechanization of our agriculture, has provided manpower for industry, transportation, and other economic activities. This redeployment of manpower has made possible our relatively advanced economy and standard of living. Much of this development stems directly from the research and teaching of America's agricultural engineers.

A total of 45 colleges and universities in the United States and Canada offer professional curriculums in agricultural engineering. Of these schools, the offerings in agricultural engineering of 25 of them are accredited by the Engineers' Council for Professional Development. Although there are around 300 graduates in agricultural engineering each year from these 45 schools, the present and longer range outlook calls for at least 3 times as many in this expanding field.

The program of the 3-day 50th anniversary meeting of the American Society of Agricultural Engineers is built around the theme "Looking to the future." Technical sessions in the four major divisions of the society—power and machinery, rural electrification and processing, farm structures, and soil and water—will follow this general theme. In addition, general sessions will deal with the role of the scientist and engineer in food and fiber production in world agriculture, manpower and energy, and the advancing front of science.—HAROLD E. PINCHES, *Agricultural Research Service, U.S. Department of Agriculture, Washington, D.C.*

Bell Laboratories researchers Henry S. McDonald, Dr. Eng. from Johns Hopkins, and Max V. Mathews, Sc.D. from M.I.T., examine magnetic tape used in new research technique. Voice waves are converted into sequences of numbers by periodic sampling of amplitudes, 8000 samples per second. General purpose electronic computers act on these numbers as a proposed transmitting device might.

They send real voices on imaginary journeys

In their quest for better telephone service, Bell Laboratories researchers must explore many new devices proposed for the transmission of speech signals. For example, apparatus can be made to transmit speech in the form of pulses. But researchers must always answer the crucial question: how would a voice sent through a proposed device sound to the listener?

In the past it often has been necessary to construct costly apparatus to find out. Now the researchers have devised a way to make a high-speed electronic computer perfectly imitate the behavior of the device, no matter how complicated it may be. The answer is obtained without building any apparatus at all.

The researchers set up a "program" to be followed by the computer. Actual voice waves are converted into a sequence of numbers by sampling the waves 8000 times per second. Numbers and program are then fed into the computer which performs the calculations and "writes out" a new sequence of numbers. This new sequence is converted back into real speech. Listeners hear exactly how well the non-existent device could transmit a real voice.

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Right Heart Catheterization

Its Contributions to Physiology and Medicine

Dickinson W. Richards

The study of the right heart in man has held a continuing place in the researches of Andre Cournand and myself over the past 25 years, both under physiological and pathological conditions. Measurements made in this exact location have provided a key to almost all the integrations that we have attempted in elucidating the nature of cardiopulmonary function.

In the realm of pathology, pulmonary heart disease also occupies a key position, affected as it is by all manner of pulmonary, as well as circulatory, dysfunctions. With many of these we are particularly concerned in our research studies of the present day.

Using these two subjects as a central theme, I should like to give a brief account of our research from its beginning.

Background in Physiology

The origins of any systematic research are many, extending widely, as well as far back in time. Many also are the supporting and sustaining research activities which are in progress simultaneously. We find ourselves deeply indebted to our colleagues throughout the world for such assistance over many years. We wish to acknowledge also the institutions which have given us financial support, especially the Commonwealth Fund, the Life Insurance Medical Research Fund, and the United States Public Health Service.

The foundation upon which the research of Cournand and myself chiefly rests is the work of Lawrence J. Henderson of Harvard University. Biochemist, physiologist, natural philosopher, student of Arrhenius, ardent disciple of Claude Bernard, Henderson achieved as his great single contribution the definitive integration of the respiratory function of the blood (*1*). But his horizon was far wider than this. He was a general physiologist in the broadest sense. For him the physical chemistry of the blood was but a single link in the whole circulorespiratory synthesis. Such breadth of view was inherent in everything he thought or did, and this could not help but be reflected, in some degree, in those whose good fortune it was to be associated with him. It was from Henderson that we derived the simple but essential concept that lungs, heart, and circulation should be thought of as one single apparatus for the transfer of respiratory gases between the outside atmosphere and the working tissues.

This concept was, of course, not new; it was in fact in the great tradition of Krogh, of Lindhard (*2*), of Liljestrand (*3*, *4*) and their collaborators, who with the methods then available, worked out to a remarkable extent in man the performance of the normal cardiorespiratory apparatus, in rest and exercise. Liljestrand made also a number of studies in disease. In the late 1920's and early 1930's the active research team at the Harvard Fatigue Laboratory under Henderson continued this exploration of cardiocirculatory patterns (*1*), to which their complete studies of the respiratory function of the blood constituted an important contribution.

During all this time, however, and indeed for a total period of nearly 40 years, there was in the study of the heart and circulation in man one measurement or set of measurements which was conspicuously in default—namely, the state of the blood as it enters the right heart, its respiratory gas contents, its pressure relations, and its rate of flow.

Although the full potentialities of these measurements were not then appreciated, it was well known that an accurate figure for the respiratory gases in the mixed venous blood would, under conditions of a physiological steady state, permit a reliable measurement of total blood flow through the lungs. The principle was the simple one originally stated by Fick (*5*) of dividing the arteriovenous difference—the amount of oxygen taken up (or carbon dioxide given off) by a unit volume of flowing blood—into the total amount of this gas taken up (or given off) by the lungs per minute.

Only those who have worked through all or a part of those times can appreciate how ardently this information was sought after, and by how many devious approaches. The majority of these involved the use of the lungs as a tonometer, equilibrating the oxygen or the carbon dioxide of the lungs with that of the incoming pulmonary arterial blood. The early experiments of Loewy and von Schrötter (*6*), the rebreathing techniques of Plesch (*7*) later of Christiansen, Douglas, and Haldane (*8*), and of Yandell Henderson (*9*), were among the more important of these.

Early Investigations

I give special emphasis to this in the present account because it was to this long-standing problem that Cournand and I applied ourselves when we began

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Dr. Richards is Lambert professor of medicine at the College of Physicians and Surgeons, Columbia University, New York, and director of the First Medical Division of Bellevue Hospital, New York. This article is based on the lecture he gave when he was awarded the Nobel prize in medicine and physiology for 1956, a prize which he shared with W. Forssmann and A. Cournand. The three Nobel lectures in physiology and medicine for the year 1956 were given at the Caroline Institute, Stockholm, on 11 Dec. 1956. Dr. Forssmann spoke first, describing earlier attempts at cardiac catheterization, his own successful experiments beginning in 1929, and the further use of the technique immediately thereafter. Dr. Richards followed, and in his lecture gave an account of the development of the work of Dr. Cournand and himself, over the 25 years of their collaborative effort. Dr. Cournand's lecture, finally, presented specifically one of the important aspects of their research—namely, the physiology of the pulmonary circulation, discussing both the present state of knowledge, and certain still unanswered problems. Dr. Richards' lecture is published here with the permission of the Nobel Foundation. Dr. Cournand's lecture will appear next week.

our work in 1931, in the service of James Alexander Miller in Bellevue Hospital. There was nothing original in our approach. We simply tried, as others had done before, to establish gaseous equilibrium between lungs and blood by rebreathing procedures, and to do this especially in patients with chronic pulmonary disease. But as others had also found before us, diseased lungs would not mix air evenly, and after 3 years it became apparent that we had failed completely in these attempts (*10*).

And yet the failure was not quite complete. There proved to be some highly interesting things about uneven mixing in diseased lungs. Robert Darling, working with us, extended earlier work in the same field by developing a breath-by-breath analysis of intrapulmonary mixing of inspired air, using the simple method of washing out intrapulmonary nitrogen through inhalation of pure oxygen (*11*). This subject has since been further studied by many investigators, and it now constitutes an important branch of pulmonary physiology. In our early experiments with Darling, two immediately practical features were worked out: an open-circuit method of measuring residual lung volume, and in the same procedure, a rough but useful index of intrapulmonary mixing—namely, the nitrogen remaining in the lungs after oxygen breathing (*12*).

At this time also, with Eleanor Baldwin we were developing other practical methods of measuring pulmonary functions, greatly aided here by similar work in progress elsewhere, especially in the clinic of Knipping and Anthony in Hamburg (*13*, *14*). By the late 1930's, we were able to describe the ventilatory functions of the lungs, and, with pulmonary measurements supplemented by arterial blood studies, in rest and exercise, to define to some extent the mixing and the diffusional aspects of pulmonary alveolar or alveolar-capillary functions (*15*). But we still could not measure blood flow through the lungs and could not, therefore, move into those broader concepts of cardiopulmonary function which now began to be our goal.

Catheterization of the Right Heart

We were aware of the earlier experiment of W. Forssmann (*16*) and had followed closely its isolated uses in Germany, Portugal, South America, and France. Dr. Forssmann has given an excellent review of this in his Nobel lecture. It suffices for me to say that, late in 1940, Cournand and Ranges (*17*) took up the catheterization technique, showing in their initial studies that consistent values for blood gases could be obtained from the right atrium and that, with this, cardiac output could be reliably and fairly accurately determined by the Fick principle, and, furthermore, that the catheter could be left in place for considerable periods without harm. Not long after, through the interest of Homer Smith and the assistance of Bradley, pressure recordings by a Hamilton manometer were added to the other techniques. Blood volumes by Gregersen's method were also included (*18*).

By this time, therefore, after 10 years of work, we had assembled a fairly comprehensive group of methods for the analysis of cardiopulmonary function, methods which could be applied not only to normal men but to patients even in the most severe and acute stages of decompensation.

Traumatic Shock

The stage was now set for study of cardiac and pulmonary functions in many forms of clinical disease. First to be undertaken was an investigation of traumatic shock in man (*18*, *19*). The United States was by this time at war, and further information on the hemodynamics of shock and quantitative measurements of this and of the effects of treatment were urgently needed. These studies proceeded quite rapidly. It was demonstrated: (i) that, with a deficit of 40 to 50 percent in blood volume, there were critical depressions in cardiac output and in return of blood to the right heart, worsening as shock continued unrelieved: (ii) that peripheral resistance tended to be maintained in hemorrhage and skeletal trauma and greatly increased in severe burns; (iii) that an important corollary of this was reduced peripheral blood flow, demonstrated particularly in the case of the kidneys; and (iv) that whole blood offered great advantages over plasma as sustaining therapy. Other forms of treatment were evaluated. Vasomotor factors, problems of so-called "irreversible" shock, were approached but not solved. In certain cases of severe burn, the catheter was left in place for more than 24 hours to provide a means of intravenous treatment, with no harm resulting—a further indication of the safety of the procedure.

Even during these war years a number of basic contributions were made. Dr. Cournand (*20*) will discuss the advancing of the catheter, first into the right ventricle, and then into the pulmonary artery, permitting new measurements to be made, some of them as important physiologically as the original right atrial (*21*). In the field of clinical heart disease, cases of heart failure with high cardiac output were identified and differentiated from "low-output" failures (*22*). McMichael and Sharpey-Schafer (*23*) in London had made similar observations independently. Baldwin (*24*) studied a case of congenital heart disease with interventricular septal defect. There were numerous improvements in technique.

Congenital Heart Disease

With the cessation of hostilities in 1945, we were free to look more broadly at problems of disease. By this time, others were at work with the same procedures, in various parts of the world.

The application of cardiac catheterization to the diagnosis of congenital heart lesions was an obvious one, and a number of investigators became interested in, and pursued, this inquiry with great skill. The early studies of Cournand, Janet Baldwin, and Himmelstein (*25*) were extended by much additional work by Bing (*26*), Dexter (*27*) and others. It should be noted that the great advance represented by the surgery of congenital heart disease, under such men as Gross (*28*), Blalock (*29*), Crafoord (*30*), and Brock (*31*), was under way before cardiac catheterization, and that it has moved fundamentally on its own. The cardiac catheter has been, however, a primary aid. Sharing with angiocardiography the ability to define the anatomical lesions, the catheter also quantitates the volumes and pressures of abnormal flow, thus defining for the surgeon both the nature and extent of the disorder. By repeated catheterization, the degree to which a normal circulation has been restored can be determined postoperatively.

Congestive Heart Failure

The measurements now available were adequate for a more general study of the physiology of heart failure; particularly since these could be carried out under conditions of cardiac decompensation and again following recovery. Pressures and flow in the pulmonary circulation gave an index of performance of the left ventricle; the same measurements in the right heart and in the great veins, an index of performance of the right ventricle. Many forms and degrees of failure were defined, and their responses to treatment were measured: limited or fixed cardiac output, not responding to exercise; left ventricular failure with pulmonary hypertension; right ventricular failure with systemic venous hypertension; the congestive state with high blood flow, and with low; very low cardiac output without congestion; the

dynamic effects of cardiac arrhythmias; the circulation in constrictive pericarditis (*32, 33*). The congestive state as such was established as a dominant aspect of heart failure, regardless of the level of general or regional blood flow.

An important contribution, in its therapeutic, as well as its physiological, implications, was the analysis of the action of the digitalis glucosides, by Ferrer and Harvey in our laboratory (*34*), also by McMichael and Sharpey-Schafer (*23*), by Bloomfield (*35*), and others. It was established that digitalis acts favorably only on overdilated ventricles, with excessive filling pressures and inadequate emptying; that in such hearts it acts rapidly to increase the energy of contraction, increase stroke volume, and promote adequate emptying, thus relieving the congestive state; that it performs with regular, as well as irregular, cardiac rhythms.

This large body of new knowledge of the dynamics of the circulation inevitably brought again under critical review the original Starling principle (*36*)—namely, that the energy of ventricular contraction is proportional to fiber length, that is, to diastolic ventricular volume; and that this relation holds up to a certain optimal fiber length, beyond which myocardial contraction progessively fails. Alternatively, in clinical studies, the more readily measured diastolic filling pressure has been commonly used, instead of diastolic volume, a relationship developed before Starling, by Otto Frank. In this general inquiry, contrary to the usual sequence, it was the clinical physiologists who stimulated the general physiologists to further research (*37*), and additional work in animals, especially by Hamilton (*38*), by Rushmer (*39*), and others, has added much interesting material. Many questions are still in controversy, but there would appear to be fairly general agreement that, in the normal heart under stress, the basic Starling relation is overridden by other influences, such as sympathetic control of muscle tone, the heart in exercise increasing its emptying, rather than its filling, volume; but that in the failing heart the fundamental relation between fiber length and energy of contraction may again emerge.

Mitral Stenosis

One particular form of acquired heart disease that has come under intensive study in the last 6 years is, of course, mitral stenosis. The magnificent achievement of cardiac surgeons in the partial or complete relief of this mechanical block has permitted also the comparative study of the hemodynamics of the circulation before and after this surgical procedure. Many factors are involved in the selection of patients for surgery (*40*). By and large, clinical improvement postoperatively has coincided with fall in pulmonary arterial pressures, and frequently with increase in resting or in exercise cardiac output. The total physiological readjustment, however, is a complex one, and the interrelations between cardiac output, pulmonary and systemic pressures, and ventilatory and other pulmonary functions have not yet been fully worked out. Among many important contributors in this field may be mentioned Ellis (*41*), Werkö (*42*), Dexter, Soulié, Donald, and Lequime.

The further extensions of the catheterization technique that are now being made, exploring the left atrium, the left ventricle, and the systemic aorta, are beyond the scope of this discussion.

Pulmonary Physiology—Diffusion

These numerous excursions into cardiac physiology, which I have just reviewed, have indeed been a major feature of our work, and yet they somewhat obscure the fact that Cournand and I have from the beginning thought of ourselves as primarily pulmonary, rather than cardiac, physiologists. I should like to outline now, though in the briefest possible terms, some of the aspects of clinical pulmonary physiology that have also been under study in our laboratory during the past several years.

I return for a moment to the work of our former colleague, the late Eleanor Baldwin, and in doing so wish to pay tribute to her for the vital part that she played in our whole research achievement. With the group of standard methods to which I have referred, she studied over a 10-year period a large number and variety of cases of chronic pulmonary disease. Inclusion of circulatory data from cardiac catheterization in many of these patients completed the picture of cardiorespiratory failure. It was found that these cases on analysis fitted well into the broad categories of pulmonary insufficiency that we had earlier described: the gross ventilatory, with restrictive or obstructive aspects; and the alveolar-capillary, with primary disturbances in respiratory gas exchange. Some disorders, such as pulmonary emphysema, were complex with various combinations of these factors. One definitely new physiological group emerged, that of the diffusional insufficiency or alveolar-capillary block, with the major interference at the alveolar-capillary interface (*43*).

This type of broad physiological analysis, with subsequent therapy directed to precise and specific aspects of insufficiency, has proved to be of great value in the clinical management of this large category of chronic disease.

In the past decade there has developed a much more exact analysis of intrinsic pulmonary function, to which I can refer here only briefly and inadequately. It is a development, however, which constitutes one of the most significant advances in basic physiology that have been made in the various fields to which cardiac catheterization has contributed. The general subject is that of diffusion of gases across the alveolar-capillary membrane and of the ventilation-perfusion relationships in the lungs. Two independent groups of investigators have been largely responsible for this development. At the University of Rochester, Rahn and Fenn (*44*) approached the subject initially by way of a description of the various possible relationships between oxygen uptake and carbon dioxide elimination in the lungs—the respiratory exchange ratio. The other, consisting first of Riley and Lilienthal, and later of Riley, Cournand, Donald, and associates (*45*), developed first a simple formula for the determination of mean alveolar oxygen tension, then proceeded to study the special properties of the oxygen dissociation curves of blood. Using the principle that at high oxygenation, equilibrium of oxygen between air and blood is complete, whereas at low oxygenation there is a distinct alveolar-capillary oxygen gradient, they found it feasible to use high and low oxygenations in human subjects to measure the diffusion process. Extension of the work led to a general definition of ventilation-perfusion relationships, separating effective "alveolar" ventilation from ineffective "dead space" ventilation, on the one hand, and effective "alveolar" perfusion from ineffective "venous admixture," on the other. Developments in this field, under Riley, Comroe and Forster, Rossier, and others, cannot be further reviewed here.

Pulmonary Heart Disease

The discussion up to this point has indeed been an overlong introduction to the problem of pulmonary heart disease. Yet this information is not irrelevant. The heart in chronic pulmonary disease is at a crossroads, itself a consequence of both pulmonary and cardiocirculatory disturbances.

Pulmonary heart disease—cardiac hypertrophy and dilatation secondary to disease of the lungs, or cor pulmonale—was clearly delineated by Laennec nearly 150 years ago, but it has attracted considerable attention only within the past generation. Its importance and its incidence are increasing, in large part because patients with chronic pulmonary disease now live longer, being protected

somewhat from infection, and relieved and sustained, in some instances for considerable periods, by symptomatic therapy.

At the present time, a very considerable proportion of patients suffering from chronic pulmonary disease with progressing pulmonary insufficiency will eventually develop cor pulmonale. In some instances, the heart failure becomes chronic and continues for years; in others it appears only terminally; in still others there may be repeated episodes of right heart strain and failure, especially during recurring pulmonary infection. These clinical patterns are only now beginning to be defined, as the cases are followed over many years; as yet, a generally accepted classification of pulmonary heart disease has not been made. In the present brief sketch, I shall move rapidly through some of the more frequently encountered forms, their natural history and physiological components. This description is based chiefly on the work of Harvey and Ferrer (*46*) in our laboratory.

It will be convenient to use as a prototype chronic diffuse pulmonary emphysema, concentrating on the features concerned with the flow of blood through the lungs and the action of the right heart.

The principal factors inducing right ventricular strain, hypertrophy, and failure can be stated very simply: (i) pulmonary hypertension, from one cause or another; and (ii) secondary influences throwing a burden on the right heart, such as anoxia, increased blood volume, polycythemia, increased cardiac output, disordered breathing mechanics.

The division of pulmonary emphysema, as originally made by Baldwin *et al.* (*43*), into four physiological groups, is applicable also to a consideration of cor pulmonale. We assume here the most common pathogenic form of emphysema, that proceeding from chronic bronchitis and bronchial obstruction, moving on to the hyperinflated obstructive type of ventilatory insufficiency.

In the first and mildest of these groups, the disturbances of pulmonary mechanics are not associated with arterial hypoxia or difficulties with elimination of carbon dioxide. In these cases pulmonary vascular pressures are within normal limits and there is no significant right heart strain (*21*).

In the second group, ventilatory function is more severely curtailed, often to one-fourth or one-fifth of normal, and anoxia appears. Work or effort of breathing is much increased. Carbon dioxide elimination is still adequate. It is extraordinary in some cases how much destruction of pulmonary tissue can exist and how little the remaining effective diffusing area is with the lungs still able to carry on carbon dioxide exchange.

Similarly, pulmonary arterial pressures can remain normal, at least during rest, with a remarkably small proportion of available vascular channels. In general, pulmonary arterial pressures seem to rise roughly in proportion to the degree of arterial hypoxia (*32*). That this is due in large part to the constricting effect of anoxia on the pulmonary vascular apparatus is suggested by the fact that, physiologically, this hypertension is frequently reversible when the patient's compensation has been restored and the anoxic state relieved. On the negative side, we have found not too clear a correlation between the degree of pulmonary hypertension and the extent of anatomical pulmonary vascular change, either muscular hypertrophy or arteriosclerosis. Clinically, the right heart often begins to show objective evidence of hypertrophy and dilatation when pulmonary arterial pressures exceed twice normal values.

In the next or third group, anoxia is more profound and carbon dioxide retention with hypercapnea is added. The aeration of the alveolar spaces has entered its final stage of decompensation, and the full state of alveolar hypoventilation is established. Here the primary constricting effects of anoxia send the pulmonary arterial pressures to higher levels; and secondary effects of both anoxia and hypercapnea place their added burdens on the heart.

The extent of breakdown here, actually of reversal of supposedly homeostatic mechanisms, is remarkable. Profound arterial oxygen unsaturation leads to marked polycythemia, total blood volume increasing by the amount of the increased red cell mass. This overfills the blood bed, including the heart, and this drives the heart, so to speak, to increased output and eventual failure. The pulmonary vascular channels may also be congested, with further anoxia resulting. That this is not a favorable homeostasis, but an unfavorable excess response, can be shown directly by a phlebotomy, which often brings immediate and striking improvement in all functions.

Even more widespread are the systemic effects of elevated carbon dioxide. The rise in alveolar and blood carbon dioxide tensions produces at the kidneys, as is shown by the work of Pitts (*47*) and of Gilman (*48*), a retention of bicarbonate, thus further raising blood and tissue carbon dioxide levels, though, of course, relieving in part the uncompensated gaseous acidosis. Continued high carbon dioxide tension apparently depresses the sensitivity of the respiratory center to the carbon dioxide stimulus, although recently some question regarding this effect has arisen. What further effects the retained bicarbonate may have on electrolyte and water balances in the body is not known.

Most extreme of the forms of physiological dysfunction in emphysema are those rather uncommon cases of severe alveolar hypoventilation, sometimes called the Ayerza syndrome, in which all the afore-mentioned trends are manifested to maximum degree, and yet sometimes with only mild anatomical changes in the lungs (*43*). Functionally, however, there is always bronchial obstruction, marked alveolar hypoventilation (*49*), and the most severe disturbances of ventilation and perfusion. Even in these cases, the entire circulation can often be restored to normal, with normal pulmonary arterial pressures and cardiac output reduced to normal values, by vigorous symptomatic therapy, relieving bronchial obstruction, hypoxia, hypercapnea, polycythemia and hypervolemia, and by active treatment of congestive failure.

There are other forms of pulmonary disease in which cor pulmonale is a significant complication. There is a category, for example, in which there has been a progressive loss of function or a destruction of total pulmonary tissue, down to a critical level, to an irreducible minimum. Cor pulmonale with failure may develop in such cases, usually terminally or as a very late stage (*50*). Such cases include those of severe kyphoscoliosis, occasionally widespread and far advanced pulmonary tuberculosis, some cases of bullous emphysema with replacement or compression of active lung tissue. I mentioned in a preceding section another newly defined form of pulmonary dysfunction, that of diffusion insufficiency or alveolar-capillary block. Such cases, in the advanced stages with continuous hypoxia, commonly have right-sided heart failure as a late complication. Still another important type is that of primary pulmonary vascular narrowing, represented by multiple pulmonary embolization, pulmonary schistosomiasis, and the somewhat controversial entity called primary pulmonary hypertension. In these the right heart strain is directly proportional to pulmonary hypertension, and the patients go eventually into massive right heart failure with low and diminishing cardiac output (*49*).

Conclusions

I have dealt with this particular subject, pulmonary heart disease, in somewhat greater detail than the rest of my account, partly to show the type of functional analysis that can readily be made in clinical cases, but partly also to illus-

trate what is perhaps obvious, that such analysis is at best superficial, does no more at the present time than set forth what some of the more fundamental problems are.

It is no part of a survey such as this to predict the future, but I should like to mention a few of the areas in which we believe that further basic research might well be concentrated. Dr. Cournand will touch on an important field—namely, the pharmacodynamics of the lung, and especially of the pulmonary circulation (*20*). Another that interests me greatly would be an effort to bring together function and structure, a re-examination of pulmonary anatomy by pathologists who are aware of functions and dysfunctions. May it not be possible to obtain, by such collaborative effort, more fundamental evidence on pathogenesis in such presently obscure and yet devastating conditions as pulmonary fibrosis in its many forms, the emphysematous change, bulla formation, the many-sided problem of pulmonary vascular change, the disorders of the bronchial circulation? Fortunately, work is already under way on many of these problems, by a new and dynamically minded generation of pathologists. So also with many of the other problems that I have touched upon, in renal and electrolyte physiology, as related to pulmonary disease, in blood formation, the physiology of the respiratory center, and so on.

I have endeavored to present in this review a brief account of the development of cardiac catheterization in our hands and some of the adventures that we have had with it. These have carried the work into many aspects of cardiopulmonary physiology and pathology. Our findings have been for the most part preliminary, revealing new problems more often than solving old ones. Of great value has been the interest which has been aroused and the excellent new work that has been stimulated in many laboratories and clinics in many countries.

References

1. L. J. Henderson, *Blood: a Study in General Physiology* (Yale University Press, New Haven, Conn., 1928).
2. A. Krogh and J. Lindhard, *Skand. Arch. Physiol.* 27, 100 (1912).
3. G. Liljestrand and J. Lindhard, *ibid.* 39, 64 (1920); 39, 215 (1920).
4. G. Liljestrand and N. Stenström, *Acta Med. Scand.* 63, 99 (1926).
5. A. Fick, *Sitzber. physik.-med. Ges. Wurzburg* 16 (1870).
6. A. Loewy and H. von Schrötter, *Z. Exptl. Pathol. Therap.* 1, 197 (1905).
7. J. Plesch, *ibid.* 6, 380 (1909).
8. J. Christiansen, C. G. Douglas, J. S. Haldane, *J. Physiol. (London)* 48, 244 (1914).
9. Y. Henderson and A. L. Prince, *J. Biol. Chem.* 32, 325 (1917).
10. D. W. Richards, A. Cournand, N. A. Bryan, *J. Clin. Invest.* 14, 173 (1935).
11. R. C. Darling, A. Cournand, D. W. Richards, *ibid.* 23, 55 (1944).
12. A. Cournand *et al.*, *ibid.* 20, 681 (1941).
13. K. Jansen, H. W. Knipping, K. Stromberger, *Beitr. Klin. Tuberk.* 80, 304 (1932).
14. A. J. Anthony, *Funktionsprufung der Atmung* (Bach, Leipzig, 1937).
15. A. Cournand and D. W. Richards, *Am. Rev. Tuberc.* 44, 26 (1941).
16. W. Forssmann, *Klin. Wochschr.* 8, 2085 (1929).
17. A. Cournand and H. A. Ranges, *Proc. Soc. Exptl. Biol. Med.* 46, 462 (1941).
18. D. W. Richards, *Harvey Lectures Ser.* 39, 217 (1943–44).
19. A. Cournand *et al.*, *Surgery* 13, 964 (1943).
20. A. Cournand, *Science*, in press.
21. R. A. Bloomfield *et al.*, *J. Clin. Invest.* 25, 639 (1946).
22. D. W. Richards, *Federation Proc.* 4, 215 (1945).
23. J. McMichael and E. P. Sharpey-Schafer, *Quart. J. Med.* (N.S.), 13, 123 (1944).
24. E. deF. Baldwin, L. V. Moore, R. P. Noble, *Am. Heart J.* 32, 152 (1946).
25. A. Cournand, J. S. Baldwin, A. Himmelstein, *Cardiac Catheterization in Congenital Heart Disease* (Commonwealth Fund, New York, 1949).
26. R. J. Bing, L. D. Vandam, F. D. Gray, Jr., *Bull. Johns Hopkins Hosp.* 80, 107 (1947).
27. L. Dexter *et al.*, *J. Clin. Invest.* 26, 561 (1947).
28. R. E. Gross and J. P. Hubbard, *J. Am. Med. Assoc.* 112, 729 (1939).
29. A. Blalock and H. B. Taussig, *ibid.* 128, 189 (1945).
30. C. Crafoord and G. Nylin, *J. Thoracic Surg.* 14, 347 (1945).
31. R. C. Brock, *Brit. Med. J.* 1948I, 1121 (1948).
32. A. Cournand, *Circulation* 2, 641 (1950).
33. D. W. Richards, *Am. J. Med.* 6, 772 (1949).
34. R. M. Harvey *et al.*, *ibid.* 7, 439 (1949).
35. R. A. Bloomfield *et al.*, *J. Clin. Invest.* 27, 588 (1948).
36. S. W. Patterson, H. Piper, E. H. Starling, *J. Physiol. (London)* 48, 465 (1914).
37. D. W. Richards, *Am. J. Med.* 3, 434 (1947).
38. W. F. Hamilton, *Circulation* 8, 527 (1953).
39. R. F. Rushmer, *Physiol. Revs.* 35, 138 (1955).
40. M. I. Ferrer *et al.*, *Circulation* 12, 7 (1955).
41. L. B. Ellis and D. E. Harken, *ibid.* 11, 637 (1955).
42. L. Werkö *et al.*, *Ann. Surg.* 133, 290 (1952).
43. E. deF. Baldwin, A. Cournand, D. W. Richards, *Medicine* 27, 243 (1948); 28, 1 (1949); 28, 201 (1949).
44. H. Rahn, *Am. J. Physiol.* 158, 21 (1949).
45. R. L. Riley and A. Cournand, *J. Appl. Physiol.* 4, 78 (1951); R. L. Riley, K. W. Donald, A. Cournand, *ibid.* 4, 102 (1951).
46. R. M. Harvey *et al.*, *Am. J. Med.* 10, 719 (1951).
47. P. J. Dorman, W. J. Sullivan, R. F. Pitts, *J. Clin. Invest.* 33, 82 (1954).
48. P. Brazeau and A. Gilman, *Am. J. Physiol.* 175, 33 (1953).
49. P. H. Rossier, A. Bühlmann, K. Wiesinger, *Physiologie und Pathophysiologie der Atmung* (Springer, Berlin, 1956).
50. A. P. Fishman and D. W. Richards, *Am. Heart J.* 52, 149 (1956).

Mechanisms of Oxygen Metabolism

H. S. Mason

Application of tracer techniques to biochemistry has often been followed by fresh insight, sometimes at a level of generalization. In the study of oxygen metabolism, which has been badly prejudiced by the influence of the expression "$\frac{1}{2}$ O_2," the use of oxygen-18 as a tracer has become broadly feasible only recently. Formerly, it was difficult to recover oxygen quantitatively from organic compounds in a form suitable for mass spectrometric analysis, but this problem was largely solved in 1953 by Doering and Dorfman (*1*).

Since then, the mechanisms of action of a number of enzymes that catalyze reactions of molecular oxygen ("oxidases") have been examined by means of tracer oxygen. The purpose of this article (*2*) is to summarize the results which have been obtained and to show that molecular oxygen is metabolized by three broad classes of enzymes, which I have named "oxygen transferases," "mixed-function oxidases," and "electron-transfer oxidases" (*3*, p. 55C; *4*).

Oxygen Transferases

By *oxygen transferase* (*5–8*) is meant an enzyme that catalyzes the consumption of one molecule of oxygen per molecule of substrate (*9*), both atoms of consumed oxygen appearing in the product (Eq. 1; the related system described by Eq. 1a is also possible, but it has not been observed).

$$S + O_2 \rightleftharpoons O_2S \qquad (1)$$

$$2S + O_2 \rightleftharpoons 2OS \qquad (1a)$$

To identify an enzyme as an oxygen transferase, it is therefore necessary to

The author is associate professor of biochemistry at the University of Oregon Medical School, Portland.

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determine the amount of oxygen consumed per molecule of substrate transformed, the amount of oxygen incorporated into the product, and, by tracer experiments, the source of the incorporated oxygen. All these tests have been carried out, and the required criteria have been met by pyrocatechase (*6*), 3-hydroxyanthranilic oxidase (*8*), and tryptophan oxidase (*8*). Some properties of these three enzymes are listed in Table 1 along with those of enzymes which have not been completely characterized but which are probably oxygen transferases.

With the exception of lipoxidase, in which the presence of a prosthetic group is still uncertain, all these oxygen transferases are metalloproteins which are activated by reducing agents and inhibited by metal-binding reagents. When it is known that ferrous iron is essential to the oxygen-transferring activity, it is reasonable to conclude that the enzymes act as iron-oxygen complexes, since the capacity of related, reduced metalloproteins (for example, hemoglobin, myoglobin, chlorocruorin, hemerythrin, and hemocyanin) to bind oxygen is well known, and since the autoxidation of heavy metals such as ferrous iron appears to take place through the formation of intermediate complexes of iron and oxygen. In any case, molecular oxygen is transferred to substrate without exchange with solvent oxygen, so that the formation of ternary enzyme-oxygen-substrate complexes, followed by rearrangement to enzyme and product, appears probable (Eqs. 2 to 4).

$$E + O_2 \rightleftharpoons EO_2 \quad (2)$$

$$EO_2 + S \rightleftharpoons EO_2S \quad (3)$$

$$EO_2S \rightleftharpoons E + O_2S \quad (4)$$

Mixed-Function Oxidases

I mean by *mixed-function oxidase* an enzyme that catalyzes the consumption of one molecule of oxygen per molecule of substrate; one atom of this oxygen molecule appears in the product, and the other undergoes a two-equivalent reduction (Eq. 5).

$$SH + O_2 + 2e \rightleftharpoons SOH + O^{--} \ (H_2O) \quad (5)$$

To identify an enzyme as a mixed-function oxidase, it is necessary (i) to determine the amount of oxygen consumed per molecule of substrate transformed, (ii) to determine the amount of oxygen incorporated into the product, (iii) to determine the source of the incorporated oxygen, and (iv) to show that two reducing equivalents are also consumed during the reaction. Since enzymes of this class catalyze, in effect, two reactions of oxygen (transfer and reduction), it is particularly important, if difficult, to establish the homogeneity of the active centers.

Table 1. Characteristics of oxygen transferases. References, where given in column 1, identify studies made with tracer oxygen.

Name	Activators	Inhibitors	Essential groups
Homogentisate oxidase	Ascorbate, glutathione, ene-diols	Dipyridyl, CN^-, iodoacetate, diethyldithio-carbamate (*p*H 5—loss of Fe^{++})	Fe^{++}, SH
Pyrocatechase (*6*)	Glutathione	Ag^+, Cu^{++}, dialysis	Fe^{++}
3-Hydroxyanthranilic oxidase (*8*)	Ascorbate	Dipyridyl, CN^-, *p*-chloromercuribenzoate, H_2O_2	Fe^{++}, SH
Protocatechuic acid oxidase		*p*-Chloromercuribenzoate	Fe^{++}, SH
Tryptophan oxidase (*8*)	H_2O_2 (?)	Catalase, CO (light reversible), N_3^-, CN^-, Cu^+	Heme (?)
Indolylacetic oxidase	Mn^{++}, monophenols, aniline (peroxidase substrates)	Catalase, CO (light reversible), CN^-	Heme
Indole oxidase	Glutathione, B_{12}, folic acid, adenylic acid	Cyanide, Azide, dipyridyl, Ag	Heavy metal
Lipoxidase			

No enzyme has been shown rigorously to be a mixed-function oxidase, for this requirement has not been adequately satisfied, but a number of enzymes are probably members of this class because they possess several, if not all, of the required characteristics. These characteristics are listed in Table 2. Of this group, imidazoleacetic oxidase (*8*), nonspecific liver hydroxylase (*10*), steroid 11β-hydroxylase (*11*), squalene oxidocyclase I (*12*), and the phenolase complex (*4*) have been studied with heavy oxygen, as has the model hydroxylating system that consists of ferrous iron and ascorbic acid in the presence of molecular oxygen (*13*).

The order in which one atom of the oxygen molecule is transferred to the substrate and the other atom is reduced is an interesting problem which has not been solved for any oxidase of this class. If the electron donors function by means of two one-equivalent reduction steps, then the free radicals O_2^- or HO_2 (but not OH), as complexes with enzyme, may be oxygen-transferring intermediates. If the donors function by means of one two-equivalent reduction, the enzyme complexes of O_2, O_2^{--}, or O may be oxygen-transferring intermediates. These alternatives are illustrated by the following reaction types. In type i mechanisms (Eq. 6)

$$EO_2 \cdot AH \cdot DH \rightleftharpoons AOH + E + D^+ + OH^- \quad (6)$$

a quaternary complex, $AH \cdot E \cdot O_2 \cdot DH$, forms and dissociates into the products AOH, D, E, and OH^- (where AH represents oxygen acceptor and DH the electron donor). If the oxygen acceptor, AH, or the product of oxygen acceptance, AOH, serves as the electron donor, as appears to be the case with the phenolase complex and *p*-hydroxyphenylpyruvate oxidase, only ternary complex formation is required.

According to the type ii mechanism, the oxygen-transferring intermediate is enzyme-oxygen complex, EO_2, which is transformed into EO as a result of transfer of one atom of oxygen to substrate (Eq. 7)

$$EO_2 + AH \rightleftharpoons AOH + EO \quad (7)$$

In a second (and possibly third) step, the electron donor reduces EO to $E + O^{--}$ (Eq. 8)

$$EO + DH \rightleftharpoons E + D^+ + OH^- \quad (8)$$

In the type iii mechanism, one oxygen atom of enzyme-oxygen complex is reduced to O^{--}, forming the oxygen-transferring intermediate, EO, Eqs. 9, 10).

$$EO_2 + DH \rightleftharpoons EO + D^+ + OH^- \quad (9)$$

$$EO + AH \rightleftharpoons E + AOH \quad (10)$$

In the type iv mechanism, the oxygen-transferring intermediate is the enzyme-peroxide complex, $E \cdot H_2O_2$ or its equivalent, formed by two-equivalent reduction of enzyme-oxygen complex (Eqs. 11, 12).

$$EO_2 + DH \rightleftharpoons E \cdot HO_2^- + D^+ \quad (11)$$

$$E \cdot HO_2^- + AH \rightleftharpoons E + AOH + OH^- \quad (12)$$

Mixed-function oxidation in which the oxygen-transferring intermediate is formed by a one-equivalent reduction step is illustrated by type v (Eq. 13).

$$EO_2 + DH \rightleftharpoons EO_2H + D \quad (13)$$

The enzyme-oxygen complex undergoes a one-equivalent reduction to $E \cdot O_2^-$ or $E \cdot O_2H$, the oxygen-transferring intermediate. The complex EO^- or EOH

that is formed as a result of oxygen transfer (Eq. 14)

$$EO_2H + AH \rightleftharpoons EOH + AOH \quad (14)$$

undergoes a second one-equivalent reduction to free enzyme and hydroxyl anion (Eq. 15).

$$EOH + D \rightleftharpoons E + D^+ + OH^- \quad (15)$$

Evidence has developed from study of the reaction complexes of hemoproteins with peroxide (*14*) and from examination of the mechanisms of aromatic hydroxylation taking place in the presence of ferrous iron, oxygen, and ascorbic acid (*13*) or peroxidase, oxygen, and dihydroxyfumarate (*15*) which strongly suggests that it is possible to form positively charged oxygen-transferring species of the general structure $Fe^{++}O$ or its equivalent, but it is not possible to generalize from this evidence to the mixed-function oxidases as a class. Much work remains to be done in this field.

Electron-Transfer Oxidases

The third major class of enzymes which catalyze reactions of molecular oxygen are the *electron-transfer oxidases*. In the presence of these enzymes and appropriate electron donors, oxygen is reduced to hydrogen peroxide (two-electron transfer, Eq. 16)

$$O_2 + 2e \rightleftharpoons O_2^{--} (= H_2O_2) \quad (16)$$

or to water (four-electron transfer, Eq. 17)

$$O_2 + 4e \rightleftharpoons 2O^{--} (= 2H_2O) \quad (17)$$

These oxidases may reduce molecular oxygen only (for example, uricase and cytochrome oxidase); in this case they are oxygen-obligative. If other electron acceptors also serve as substrates (as with glucose oxidase, xanthine oxidase, and others) they are oxygen-facultative. In order to identify an enzyme as an electron-transfer oxidase, it is necessary to show that one molecule of oxygen is consumed per two electrons transferred and that the product is hydrogen peroxide (Eq. 16) or that one molecule of oxygen is consumed per four electrons transferred and that the product is water (Eq. 17). If, as a result of electron loss, the donor molecule is ultimately oxygenated (as with uric acid and xanthine oxidations) it must be shown that the incorporated oxygen atoms arise from the solvent or from oxyanions dissolved in the solvent (Eq. 18; Eq. 19 describes one possible mechanism for this kind of reaction)

$$O_2 + DH + OH^{--} \rightleftharpoons HO_2^- + DOH \quad (18)$$

$$DH \rightleftharpoons D^+ + H^+ + 2e \quad (19)$$
$$D^+ + OH^- \rightleftharpoons DOH$$

whereas hydrogen peroxide and water formed by these electron transfers must be derived from the atoms of molecular oxygen which have been consumed. A list of the various classes of electron-transfer oxidases follows.

Two-electron transfer, oxygen obligative. Uricase (*16*).

Two-electron transfer, oxygen-facultative. Xanthine oxidase (*17*), aldehyde oxidase, glucose oxidase (*18*), arabinose oxidase, pyruvic oxidase, glycolic oxidase, α-hydroxyacid oxidase, acyl CoA dehydrogenase, monamine oxidase, diamine oxidase, sarcosine oxidase, N-methylamino oxidase, diphosphopyridine nucleotide oxidase, methemoglobin reductase, triphosphopyridine nucleotide oxidase, triphosphopyridine nucleotide-cytochrome reductase, pyrimidine oxidase, and others.

Four-electron transfer oxidases. Laccase, catecholase function of phenolase complex, ascorbic acid oxidase, and cytochrome oxidase.

There are experimental obstacles which make it difficult, if not impossible, to determine whether these enzymes transfer hydrogen as well as electrons to oxygen. In the case of pyridine nucleotide acceptors for two-electron transfer oxidases, transferred hydrogen is fixed and can be detected by tracer techniques, but when molecular oxygen is the electron acceptor, hydrogen which might have been transferred during the formation of hydrogen peroxide or water is readily exchangeable with solvent protons and cannot be identified. For this reason, the expression *electron-transfer oxidase* is preferred.

During formal stepwise addition of two electrons to molecular oxygen, a very reactive free radical intermediate, O_2^- or HO_2 (perhydroxyl) may be formed, and during the formal stepwise addition of four electrons to molecular oxygen, both perhydroxyl and free hydroxyl may form (Eqs. 20 to 23)

$$O_2 + e \rightleftharpoons O_2^- \text{ or } HO_2 \quad (20)$$

$$HO_2 + e \rightleftharpoons HO_2^- \text{ or } H_2O_2 \quad (21)$$

$$H_2O_2 + e \rightleftharpoons H_2O_2^- \text{ or } H_2O + \cdot OH \quad (22)$$

$$\cdot OH + e \rightleftharpoons OH^- \text{ or } H_2O \quad (23)$$

From a biological point of view, enzymic reduction mechanisms that form these free radicals from molecular oxygen must be disadvantageous to the organism, not only because an energetic random attack on functioning components and structures of the cell must ensue, but also because biochemically efficient utilization of the free energy of these radicals appears to be impossible. It is more likely that the whole process of oxygen reduction takes place in such a manner that intermediate unpairing of electrons, if it occurs at all, occurs under such chemical or spatial constraint that the free radicals which form are essentially independent of the random collision or mass action principle.

Since the mechanisms of enzymic two-electron and four-electron transfers to oxygen have been extensively discussed in recent articles (compare *19, 20*) only brief comment on this subject is given here. Two-electron transfers to oxygen may be catalyzed by metalloproteins (for example, uricase, xanthine oxidase, aldehyde oxidase) or by coenzyme-enzyme complexes (for example, glucose oxidase, arabinose oxidase, glycolic oxidase, amino acid oxidases, and others). In the case of the copper-containing, oxygen-obligative enzyme, uricase, evidence has been reported (*19*) which supports the view that the metal atom provides a locus for the aggregation of both urate

Table 2. Characteristics of mixed-function oxidases.

Name	Cosubstrate	Inhibitors	Essential groups
Phenylalanine hydroxylase	Diphosphopyridine nucleotide	Dipyridyl, N_3^-, CN^-	Fe^{++}
Imidazoleacetic oxidase (*8*)	Diphosphopyridine nucleotide		
Nonspecific liver hydroxylase (*10*)	Triphosphopyridine nucleotide (not DPNH, H_2O_2, or ascorbate)	Dipyridyl, *p*-chloromercuribenzoate	Fe^{++}, —SH
Steroid 11-β-hydroxylase (*11*)	Triphosphopyridine nucleotide	Versene, CN^-	Unknown
Kynurenine 3-hydroxylase	Triphosphopyridine nucleotide		Unknown
p-Hydroxyphenylpyruvate oxidase	Substrate intermediate	*p*-Chloromercuribenzoate, diethyldithiocarbamate, *N*-ethylmaleimide	Cu, SH
Phenolase complex (*4*)	*o*-Diphenolic intermediate	CO, CN^-, diethyledithiocarbamate	Cu^+
Squalene oxidocyclase I (*12*)	Di- or triphosphopyridine nucleotide		Unknown
Peroxidase hydroxylating system	Dihydroxyfumarate	Mn^{++}, catalase	Heme

and oxygen in a ternary catalytic complex, permitting the transfer of electrons, either singly or in pairs, from urate to oxygen.

Beinert has recently reported that in the oxidation of substrate by the flavoprotein, fatty acyl CoA dehydrogenase, two molecules of enzyme-bound flavin appear to act together (*21*). They are reduced together to a semiquinonoid state by one molecule of substrate which is thereby converted directly to product without passing through a detached free radical state. It is reasonable to suppose that in the reoxidation of the semiquinonoid enzyme intermediate by oxygen, two electrons are similarly transferred to the oxygen molecule without forming a detached perhydroxyl free radical. It is of interest that the oxygen-facultative, two-electron transfer oxidase, glucose oxidase, also contains two molecules of flavin per molecule of enzyme. If these coenzymes act in concert during the reduction of molecular oxygen to hydrogen peroxide without forming detached perhydroxyl, the absence of indiscriminate radical attack during the action of the enzyme may be explained.

The enzymes which catalyze terminal four-electron transfer to molecular oxygen are all metalloproteins (laccase, ascorbic oxidase, catecholase function of the phenolase complex, and cytochrome oxidase). In these cases, it is usually considered that either four consecutive transfers of single electrons to the bound oxygen molecule occur, or that the electron-transfer oxidase is so organized with respect to substrate that groups of electrons can be transferred simultaneously. This may be accomplished by means of clusters of oxidases bound to the oxygen molecule, each undergoing one-equivalent oxidation-reductions, or by means of two-equivalent (or higher) oxidation-reductions (*14*).

In the case of oxidases bearing copper or iron at their active centers, this might involve valence states higher than two or three (for example, respectively Cu^{+3}, Cu^{+4}, Fe^{+4}, Fe^{+5}, or Fe^{+6}). In such a case, two-equivalent reduction of molecular oxygen becomes possible without formation of detached free radical intermediates. The evidence mentioned concerning the reactions of hemoproteins with peroxides (*14*), and electrophilic hydroxylations catalyzed by ferrous iron-oxygen systems (*13, 15*) suggests that molecular oxygen bound to cytochrome oxidase may undergo two two-electron reduction steps, each step forming a water molecule or hydroxyl anion (Eqs. 24, 25).

$$Fe_c^{++}O_2 + 2e \rightleftharpoons Fe_c^{++}O + O^{--} \quad (24)$$

$$Fe_c^{++}O + 2e \rightleftharpoons Fe_c^{++} + O^{--} \quad (25)$$

The relationship between such a mechanism for the terminal reduction of molecular oxygen to two molecules of water and mechanisms proposed for mixed-function oxidation (types ii and iii) is apparent and is being investigated. It is also apparent that such electron transfer and mixed function systems, acting in reverse with consumption rather than production of energy, afford interesting hypotheses for photosynthetic formation of molecular oxygen.

Summary

The enzymes which catalyze reactions of molecular oxygen occur in three principle classes: (i) oxygen transferases, (ii) mixed function oxidases, and (iii) electron transferases. The first class catalyzes the transfer of a molecule of molecular oxygen to substrate. The second class catalyzes the transfer of one atom of the oxygen to substrate; the other atom undergoes two-equivalent reduction. The third class catalyzes the reduction of molecular oxygen to hydrogen peroxide or to water.

References and Notes

1. W. von E. Doering and E. Dorfman, *J. Am. Chem. Soc.* 75, 5595 (1953).
2. An extended development and discussion of the ideas proposed here is in press (*Advances in Enzymol.*). I wish to thank the U.S. Public Health Service, the American Cancer Society, and the National Science Foundation for support, at the University of Oregon Medical School, of research concerned with phases of oxygen metabolism.
3. H. S. Mason, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 55C.
4. ———, W. L. Fowlks, E. W. Peterson, *J. Am. Chem. Soc.* 79, 2914 (1955).
5. The expression *oxygen transferase* was first used (*4, 6*) in the present connection in order to maintain a historical continuity in the oxidase field. The general debate on mechanisms of biological oxidation which took place between the schools of Warburg and Wieland, among many others, was concerned in part with the problem of enzymic oxygen transfer. Since tracer study has now demonstrated that oxygen transfer does occur enzymically, the expression *oxygen transferase* is being used categorically within the limits of a specific definition given in the text. The term *oxygenase* has recently been suggested for these enzymes (*7, 8*) because it is succinct, because it is consistent with *hydrogenase* and because enzymic *transfer* is being employed in connection with groups or radicals rather than molecules. It is hoped that a consensus of interested investigators on this matter of nomenclature will soon be reached.
6. O. Hayaishi, M. Katagiri, S. Rothberg, *J. Am. Chem. Soc.* 77, 5450 (1955).
7. O. Hayaishi, personal communications.
8. O. Hayaishi, S. Rothberg, A. H. Mehler, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 53C.
9. By *substrate* is meant the reagent other than molecular oxygen, which is itself a substrate.
10. S. Udenfriend, C. Mitoma, H. S. Posner, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 54C.
11. M. Hayano *et al.*, *Arch. Biochem. and Biophys.* 59, 529 (1955); M. L. Sweat *et al.*, *Federation Proc.* 15, 237 (1956).
12. T. T. Tchen and K. Bloch, *J. Am. Chem. Soc.* 78, 1516 (1956), Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 56C.
13. H. S. Mason and I. Onoprienko, *Federation Proc.* 15, 310 (1956).
14. P. George, *Currents in Biochemical Research*, D. Green, Ed. (Interscience, New York, 1956), p. 338.
15. H. S. Mason, I. Onoprienko, D. Buhler, *Biochim. et Biophys. Acta* 24, 225 (1957).
16. R. Bentley and A. Neuberger, *Biochem. J. (London)* 52, 694 (1952).
17. I. Onoprienko and H. S. Mason, unpublished results.
18. R. Bentley and A. Neuberger, *Biochem. J. (London)* 45, 584 (1949).
19. H. R. Mahler, H. M. Baum, G. Hubscher, *Science* 124, 705 (1956).
20. H. R. Mahler, *Advances in Enzymol.* 17, 233 (1956); B. Chance and G. P. Williams, *Advances in Enzymol.* 17, 65 (1956); W. W. Wainio and S. J. Cooperstein, *Advances in Enzymol.* 17, 329 (1956).
21. H. Beinert, *Biochim. et Biophys. Acta* 20, 588 (1956).

A. G. Keller, Distinguished Sociologist

One of the great figures at Yale University for nearly half a century, Albert G. Keller, emeritus professor of the science of society, died on 31 October 1956. Born in Springfield, Ohio, he received his B.A. degree in 1896 and his Ph.D. degree in 1899, at Yale University. He immediately joined the Yale faculty and taught uninterruptedly until his retirement in 1942.

An ardent disciple of his predecessor, William Graham Sumner, who introduced, in 1875, the first course in sociology in an American university, he devoted much of his research, following the latter's death in 1910, to bringing to completion the huge project which Sumner had begun and which was finally published as the four-volume *Science of Society*, in 1927. Keller, a prodigious writer, was the author of 12 other volumes. Noteworthy among them are *Homeric Society* (1902), *Colonization* (1908), *Societal Evolution* (1915), *Man's Rough*

Road (1932), and *Net Impressions* (1942). He also edited various books—collections of Sumner's essays in particular—and published scores of articles and hundreds of notes and reviews.

Like Sumner, Keller was a pioneer in stressing the objective and scientific approach to the study of social phenomena. The two men founded what might be called "cultural sociology," a comparative study of the institutions and patterned forms of behavior of social groups. At the risk of oversimplification, it may be said that Sumner's major single contribution was the concept of the folkways (*Folkways,* 1906) and Keller's, that of extending the principle of evolution into the social range (*Societal Evolution,* 1915). Sumner defined folkways as habits of the individual and customs of the society which arise from efforts to satisfy needs. They become regulative for succeeding generations and take on the character of a social force. Although deeply rooted in tradition, they are modifiable and change in response to changing life-conditions. Keller demonstrated that adjustment is the crucial fact in social life, that man's mode of adjustment is mental and social rather than organic, and that it may be measured by his civilization or culture. Societal adjustment, he further held, is achieved, in the main, automatically, through the operation of massive impersonal forces of which the individuals concerned are rarely more than dimly aware.

The work of both scholars was integrated in the monumental *Science of Society,* which traced the development and adjustment of social institutions from early beginnings, drawing material from primitive, as well as modern, societies, and basing conclusions on tens of thousands of instances or cases.

This dispassionate analysis, classification, comparison, sequence-making, and law-derivation in the field of human affairs was a novel approach in their time, when the traditional study of mankind consisted in appeal to the supernatural, appeal to authority, reliance on intuition, pure logic, and the like, with no thought of subjecting notions to rigorous verification, and when indeed, at least in certain quarters, it was regarded as quite improper to consider men and society as natural phenomena. "Undergraduate students," Keller once wrote, "know little about method, and care less. What they imbibe, however, from tender years, is deduction, always deduction. They are not taught much about causes —impersonal causation—but ever is agency set before them, chiefly in the guise of the great man, the hero to worship. They are fed upon grand shaky major premises and imposing visions of idealized lives of great men, and other edifying and ethical mythology. Through such constructions Sumner [and Keller too] drove a mighty bludgeon. Of course there was lamentation and resistance as the pieces flew, but young men are far from being supine fools and besides, they are not averse to a racket; and many of them followed Sumner through the hole he had made and came out into a freer air on the far side."

A born teacher, with the knack of putting ideas, even abstract ones, into forceful language, Keller exerted a tremendous influence on generations of Yale students. In his long years at Yale he estimated that he had taught 16,000 of them. Teaching he regarded as a man-sized job, to be done to the best of one's ability, faithfully and conscientiously; a human job that should rank above the paper job of research and publication. He demonstrated that he could do both extremely well, but, to his mind, teaching was the greater of the two.

The distinguishing traits of his teachings, as they were impressed on his students, were to challenge every idea and tradition by reference to cold facts; to conceive present crises—political, economic, social—in the light of a long stretch of social evolution; to mistrust all panaceas, exercises in logic, and subjective and mystical revelations of ethical principles and transcendent philosophies; to dig the major premise out of every generalization, particularly out of the noble ones; to work unceasingly; never to compromise for the sake of diplomacy; and, above all, to discipline oneself.

Keller held that all good elementary teaching in college must be more or less dogmatic. "To begin with the balancing of theories," he asserted, "is idiotic. The only way in which a student may healthily set out is from some definitely and clearly presented position; then subject it to all the criticism possible. But there must be something solid to set foot upon, and I do not know what could be better adapted to the purpose than the matured conclusions, from long and intimate acquaintance with the facts, of a mind whose single interest is the truth. What matter if later study and experience cause one to question such conclusions? He has at least something positive to correct or reject; and is challenged by his very respect for what he has been strongly taught, not to abandon it for less than serious reason."

In part because of a shy and retiring nature, which he hid behind a kind of surface bluntness, and in part because he felt they took time away from his work, Keller shunned membership in professional organizations and most outside activities. Although he was one of the founders of the American Sociological Society, he attended its meetings for only a few years and later resigned. His memberships consisted only of Phi Beta Kappa, the Sigma Xi, and the university club.

A lone wolf in many respects, Keller was distinguished by his personal and intellectual honesty, which led him to deal openly with others and to abhor all political maneuvering; by his scientific integrity, which made him impatient of fools and charlatans (of whom there have been more in the social sciences than in disciplines further advanced toward preciseness); by his paradoxical combination of a fundamental tolerance of attitude with a dogmatism of exposition, which proved effective in long years of successful undergraduate teaching; by his stability and toughness of mind, his utter lack of pretense, and his austerity. Defects reside in these as in all virtues, as Keller would have been the last to deny, but the picture that emerges is that of a genuine scientist, imbued with a deep humility in the face of the mountain of the unknown beside the molehill of the known.

MAURICE R. DAVIE
Department of Sociology, Yale University, New Haven, Connecticut

News of Science

2000 Sign Test Ban Appeal

Nobel laureate Linus Pauling, head of the Division of Chemistry and Chemical Engineering at California Institute of Technology, recently released to the press a petition urging the cessation of nuclear bomb tests. The statement, called "An appeal by American scientists to the governments and people of the world," was signed initially by 27 specially solicited scientists and then circulated for further signatures among the science faculties of universities throughout the country. In the 4-day period 29 May to 1 June, approximately 2000 scientists, acting as individuals, lent their support to the appeal, which reads as follows:

"We, the American scientists whose names are signed below, urge that an international agreement to stop the testing of nuclear bombs be made now.

"Each nuclear bomb test spreads an added burden of radioactive elements over every part of the world. Each added amount of radiation causes damage to the health of human beings all over the world and causes damage to the pool of human germ plasm such as to lead to an increase in the number of seriously defective children that will be born in future generations.

"So long as these weapons are in the hands of only three powers an agreement for their control is feasible. If testing continues, and the possession of these weapons spreads to additional governments, the danger of outbreak of a cataclysmic nuclear war through the reckless action of some irresponsible national leader will be greatly increased.

"An international agreement to stop the testing of nuclear bombs now could serve as a first step toward a more general disarmament and the ultimate effective abolition of nuclear weapons, averting the possibility of a nuclear war that would be a catastrophe to all humanity.

"We have in common with our fellow men a deep concern for the welfare of all human beings. As scientists we have knowledge of the dangers involved and therefore a special responsibility to make those dangers known. We deem it imperative that immediate action be taken to effect an international agreement to stop the testing of all nuclear weapons."

The initial sponsors of the statement, in addition to Pauling, include: Barry Commoner, department of botany, Washington University; Edward U. Condon, chairman, department of physics, Washington University; Charles D. Coryell, department of chemistry, Massachusetts Institute of Technology; Leslie C. Dunn, department of zoology, Columbia University; Viktor Hamburger, department of zoology, Washington University; Michael Heidelberger, College of Physicians and Surgeons, Columbia University; I. H. Herskowitz, department of zoology, Indiana University; Herbert Jehle, department of physics, University of Nebraska; Martin Kamen, department of biochemistry, Washington University; Edwin C. Kemble, department of physics, Harvard University; I. M. Kolthoff, School of Chemistry, University of Minnesota; Chauncey Leake (physiology, pharmacology), vice president, Medical Branch, University of Texas; S. E. Luria, department of bacteriology, University of Illinois; Max Mason (mathematics), California Institute of Technology; Carl V. Moore, dean, School of Medicine, Washington University; Philip Morrison, department of physics, Cornell University; Hermann J. Muller, distinguished service professor, department of zoology, Indiana University (Nobel prize, 1946); Severo Ochoa, chairman, biochemistry department, New York University–Bellevue Medical Center; C. C. Price, director, Harrison Laboratory of Chemistry, department of chemistry, University of Pennsylvania; Arthur Roberts, department of physics, University of Rochester; M. L. Sands, department of physics, California Institute of Technology; Vernor Schomaker, department of chemistry, California Institute of Technology; Laurence H. Snyder, dean of the Graduate College and professor of medical genetics, University of Oklahoma, and president of the AAAS; Oswald Veblen, professor, school of mathematics, Institute for Advanced Study, Princeton; Maurice B. Visscher, professor of physiology and head, department of physiology, University of Minnesota; W. H. Zachariasen, department of physics, University of Chicago.

Among other signers are Joseph Erlanger of Washington University (Nobel prize, 1944), Harlow Shapley of Harvard University, and David L. Hill of the Atomic Energy Commission's Los Alamos Scientific Laboratory. Pauling reports that there are approximately 40 members of the National Academy of Sciences on the roster. However, many well-known scientists have refused to sign the petition, some with public statements of protest.

Joel H. Hildebrand, head of the department of chemistry at the University of California, commented as follows in a letter to Pauling:

"Your statement that 'each nuclear bomb test spreads an added burden of radioactive elements over every part of the world' is not a true indication of the dangers in the absence of quantitative comparisons with natural radiation and current X-ray usage. . . . Your statement goes far beyond 'making the dangers known'; it enters the realm of international diplomacy where a scientist possesses no peculiar knowledge or wisdom. . . . I think, with Dr. Willard F. Libby, that the risk to persons from radioactive fall-out should be estimated against the risk to human freedom of abandoning what appears at present to be its main defense in a world where international agreements are continually violated. Freedom was won for us by men who valued it above life; we should preserve it even at the cost of lives."

George Beadle, head of the biology department at California Institute of Technology and former AAAS president said:

"I agree there is urgent need for reviewing the situation, both scientifically and morally. . . . I feel that scientists ought to confine their public statements to their own fields, or to make it clear that they are speaking not as experts but are expressing private opinions."

Still another point of view about the appeal was presented by Bentley Glass, geneticist and professor of biology at Johns Hopkins University, who observed:

"It is important to note that this appeal does not ask for a unilateral cessation of weapons testing, but for an international agreement. That, of course, is exactly what all Americans want if it is obtainable with the proper precautions. Whether the appeal backed by the signatures of many scientists will at the present moment strengthen the hands of our representatives trying to negotiate such an agreement in London, or possibly may embarrass them, it is hard to say."

The document has been forwarded to Representative Chet Holifield (D., Calif.), chairman of the subcommittee of the Joint Congressional Committee on Atomic Energy, which has been holding hearings on the radiation problem.

Aid for Polish Science

A $475,000 appropriation to aid science in Poland has been announced by the Rockefeller Foundation. At the end of April the Ford Foundation also announced a $500,000 grant to stimulate cultural, science and technical exchanges between Poland and the West. Both programs developed from visits by the foundation's representatives to Poland last February. In each case, they were the first such efforts by the foundations on behalf of Soviet-dominated countries.

The Rockefeller program includes $175,000 for fellowships to enable from 20 to 30 young Polish scholars to study in other countries during the next year. The remaining $300,000 is to buy materials and equipment for Polish universities and research institutions. In addition, half a dozen senior Polish scholars are expected to be included in the foundation's regular program for travel grants. This would be outside the special appropriation.

Approximately half of the Polish fellows may seek to come to the United States. Problems of passports and visas will be handled by the scientists themselves. The State Department has indicated it is "the general attitude of our Government to encourage such contacts with Poland." No favors or exceptions from official policy have been asked.

The fellows will be drawn largely from the biological sciences, particularly medicine and agriculture. After personal interviews by foundation advisers with candidates nominated by Polish institutions, awards will be made that will assure the scholars posts upon their return to Poland.

The $300,000 grant will aid the universities at Warsaw, Poznan, Wroclaw, Lublin, Cracow, and Lodz, medical and agricultural schools and research institutes affiliated with the Ministries of Health and Agriculture, and the Polish Academy of Sciences.

Film on Security Practices

Can the Federal Government's industrial security program grow so large that eventually every engineer and scientist in the country will require clearance in order to work anywhere at all? This question is raised in a movie previewed recently in Washington by the national council of the League of Women Voters. The film, produced by the League's Carrie Chapman Catt Memorial Fund, neither condemns nor condones current security practices. The League's purpose in making the film is not to criticize the industrial security program, "but to get people to think about it."

"Kill Only the Ivy" is the title. It will be offered soon to League units all over the United States for local presentation. The movie shows the outcome of two fairly typical cases which actually came before the screening board set up in the Defense Department to pass on people who apply for secret and top-secret work in defense plants. In both cases dramatized, clearance had been denied. But eventually, in one instance, the decision was reversed.

Women in Engineering

Emma C. Barth, an engineer in the rotating apparatus department at the Westinghouse plant in East Pittsburgh, Pa., commented recently on discrimination against women engineers. She pointed out in a lecture that of more than 120,000 women who received degrees in 1956 only 62 were graduated in engineering, while at the same time a survey by the National Education Association showed that this country will need 630,000 engineers by 1965 but will have only 530,000 available then. Miss Barth also observed that the male advantage in basic engineering aptitude tests is only 3 to 2 over women, according to a 1956 report of the U.S. Department of Labor.

Brown-Hazen Fund

The Research Corporation has announced the establishment of the Brown-Hazen Fund, its first program of grants in the medical sciences. The fund's resources are derived from royalties on the production of nystatin, the antifungal antibiotic discovered and developed by Elizabeth L. Hazen and Rachel Brown of the scientific staff of the New York state laboratory.

The fund committee will consider requests for support of fundamental research in biochemistry, microbiology, and immunology. Inquiries may be addressed to Dr. Rachel Brown (secretary), Division of Laboratories and Research, New York State Department of Health, Albany 1, N.Y., or to Mr. Charles H. Schauer, Research Corporation, 405 Lexington Ave., New York 17, N.Y.

Pyroceram

The Corning Glass Works has reported the development of a versatile new substance, Pyroceram, that is harder than steel and lighter than aluminum. The material was announced at the recent dedication of Corning's new research center. The first practical use of Pyroceram will be in radomes, the nose cones that protect the directional instruments in guided missiles.

Pyroceram starts out as glass and is melted and fashioned in the same way. But each batch of raw material includes chemical ingredients that contain a nucleating agent, which, under heat treatment, forms crystals. Glass is noncrystalline, whereas Pyroceram is crystalline.

The new material can be cast like metal in a foundry, thus allowing the fabrication of large and complex shapes. The substance is extremely hard and fine grained. It can be made transparent or opaque and, by controlling the chemical composition and growth of the Pyroceram crystals, materials of widely differing properties can be produced. Pyroceram was invented and developed by S. Donald Stookey, manager of Corning's chemical research department.

Cloud-Seeding

An evaluation of the effects of commercial cloud-seeding that has been carried out in the Great Plains area is being conducted by the Advisory Committee on Weather Control. The problems of this evaluation are being called to the attention of interested meteorologists and statisticians before an attempt is made to calculate the precipitation during the seeded period.

At present the committee staff is studying techniques for the effective forecasting of precipitation in the summertime. The problems that present themselves immediately are (i) how to find a satisfactory control area and (ii) how to deal with the wide variability of the shower-type precipitation that occurs during the summer. Comments and suggestions will be appreciated. These should be sent to Max A. Woodbury, Advisory Committee on Weather Control, Washington 25, D.C.

Luminous Clams

William D. McElroy, professor of biology at Johns Hopkins University and director of the university's McCollum-Pratt Institute, is in Naples, Italy, collecting specimens of the luminous clam, *Pholas dactylus*, that is native to the area. Through the cooperation of the Naples Experimental Zoological Station, he hopes to procure several hundred of these mollusks, which he will have packed in ice and shipped to the university.

McElroy and his colleagues will use the clams in their studies of the conversion of chemical energy into light energy. The research group at Hopkins has long been concerned with the chemical in fireflies, adenosine triphosphate, that is

necessary for light emission. This compound, called ATP, is present in all living things and plays a part in the utilization of energy.

McElroy for a number of years has been using large quantities of fireflies' tails in his efforts to learn how energy is liberated. Through this work with fireflies, he discovered that luciferin, a compound in the firefly's tail or lantern, when combined with ATP and the enzyme luciferase, produces light. The amount of light varies with the amount of ATP; hence, the combination of small amounts of tissue of the lantern with a fixed amount of luciferin and luciferase will determine how much ATP is in the tissue. McElroy will use clams in this study for the first time.

New Nuclear Laboratory

The $50 million atomic research laboratory in Middletown, Conn., where the Air Force intends to develop a nuclear aircraft engine, received its first employees last month. Pratt and Whitney Aircraft Corporation, which will operate the laboratory for the Air Force, has moved equipment and 500 employees who have been working on the project from South Windsor, Conn., into the Maromas section of Middletown. The Air Force facility, known as CANEL, covers a 1200-acre tract in an isolated area bordering the Connecticut River. Under construction for almost 2 years, the plant will employ about 3500 when it goes into full operation late this year.

Educational TV

The Fund for the Advancement of Education (New York) has announced the establishment of the National Program in the Use of Television in the Public Schools, for which the fund is making available $986,000. Taking part in this program initially are eight large cities—Atlanta, Cincinnati, Detroit, Miami, Norfolk, Oklahoma City, Philadelphia, and Wichita—and two states, Nebraska and Oklahoma. Grants have been made to the public school authorities in these cities and states on a matching dollar basis to begin regular classroom instruction over television in the elementary and high schools. In each case television teaching to large classes will begin next September.

The fund has over the past 2 years supported a number of experiments in the use of television in the public schools—notably in Hagerstown (Md.), St. Louis, Pittsburgh, and Chicago. These demonstrations have already shown that a teacher can extend his services through the use of television, that pupils learn at least as much in television classes as with conventional instruction, that television saves a great deal of time and thus permits teachers to give pupils more individual attention. The National Program in the Use of Television in the Public Schools will try to find out whether the experience in a few communities can be applied to most American schools.

Proposed Legislation

Of the many bills introduced in Congress, some have a special relevance to science and education. A list of such bills introduced recently follows.

HR 7431. Make an appropriation to National Science Foundation to construct and equip a geophysical institute in Territory of Hawaii. Burns (D Hawaii) House Appropriations.

HR 7245. Authorize Secretary of Army, Secretary of Navy, and Secretary of Air Force to make grants to educational institutions for construction of military and naval science buildings. Rabaut (D Mich.) House Armed Services.

HR 7171. Create a Federal Advisory Council of Health in Executive Office of the President. Wainwright (R N.Y.) House Interstate and Foreign Commerce.

HR 7388. Regulate interstate distribution and sale of packages of hazardous substances intended for household use. Curtis (R Mo.) House Interstate and Foreign Commerce.

H Res 243. Express sense of House that Secretary of Health, Education and Welfare should investigate the Santa Cruz plan for rehabilitation of hospitalized mental patients. Gubser (R Calif.) House Interstate and Foreign Commerce.

S J Res 85. Amend act approved 7 Aug. 1935 (P.L. 253) concerning U.S. contributions to International Council of Scientific Unions. Green (D R.I.) (by request) Senate Foreign Relations.

HR 7167. Amend section 1314 of act of 7 Aug. 1953 (P.L. 207) 83rd Congress (67 Stat. 418) *re* authority of Federal officers and agencies to withhold information and limit availability of records. Hoffman (R Mich.) House Appropriations.

HR 7172. Amend section 3 of chapter 324 of act of 11 June 1946 (60 Stat. 238) to clarify and protect right of public to information. Dawson (D Ill.) House Judiciary.

S 1949. Facilitate the administration of the public lands. Murray (D Mont.) (by request). Senate Interior and Insular Affairs.

S 2119. Expedite utilization of television facilities in our public schools and colleges and in adult training programs. Magnuson (D Wash.) Senate Interstate and Foreign Commerce.

S 2039. Clarify the requirements *re* performance of labor imposed as a condition for the holding of mining claims on Federal lands pending the issuance of patents therefor. Bible (D Nev.) Senate Interior and Insular Affairs.

HR 7253. Amend section 27 of act entitled "An act to promote the mining of coal, phosphate, oil, oil shale, gas and sodium on the public domain" to increase the aggregate acreage of coal leases that may be held by one person in any one state. Thomson (R Wyo.) House Interior and Insular Affairs.

S 2072. Establish a Chiropractic Section in Medical Service Corps of Army. Case (R S.D.) Senate Armed Services.

HR 7542. Authorize Secretary of Navy to take possession of naval oil shale reserves and to experiment in extraction of synthetic liquid fuels from oil shale in interest of national security. Staggers (D W.Va.) House Armed Services.

HR 7444. Amend Veterans' Readjustment Assistance Act of 1952 to make educational benefits provided for therein available to all veterans, whether or not they served during a period of war or of armed hostilities. Beckworth (D Texas) House Veterans' Affairs.

S 2077. Direct Secretary of Department of Interior to undertake a survey in order to assist in promoting the production of concentrated iron ore and steel in southern Appalachian area. Talmadge (D Ga.), Russell (D Ga.), Thurmond (D S.C.), Johnston (D S.C.), Sparkman (D Ala.), Hill (D Ala.), Kefauver (D Tenn.), Ervin (D N.C.), Scott (D N.C.).

Scientists in the News

H. BURR STEINBACH, professor of zoology at the University of Minnesota, has been appointed chairman of the department of zoology at the University of Chicago, effective 1 July. He succeeds the late Carl R. Moore. Steinbach is well known for his work in bioelectric phenomena, injury potentials, the sodium-potassium equilibrium of cells, ontogenesis of enzyme systems in chicks, and the enzyme systems of cellular inclusions.

HARVEY BROOKS, investigator of nuclear power and solid-state physics, will become dean of engineering and applied physics at Harvard University on 1 Sept. Brooks, who is Gordon McKay professor of applied physics, is in England this year conducting research as a Guggenheim fellow at the Cavendish Laboratory, Cambridge.

He will succeed JOHN H. VAN VLECK, Hollis professor of mathematics and natural philosophy, who plans to resume his research in mathematical

physics. Van Vleck also expects to prepare a greatly enlarged edition of his *Theory of Electric and Magnetic Susceptibilities,* published in 1932.

MARGARET G. ARNSTEIN, who is to become chief of Public Health Nursing for the U.S. Public Health Service on 1 July, has been named the first visiting professor under the Annie W. Goodrich Endowment at the Yale University School of Nursing. She will take a leave from her Government post to teach at Yale University next spring.

CARL H. KOONTZ, professor of civil engineering at Worcester Polytechnic Institute, has been named head of the department. He succeeds the late Andrew H. Holt.

D. J. RICHEY and C. L. MORGAN, both of Clemson College, have received the annual Jefferson award of the South Carolina Academy of Science for their paper "Control of leucocytozoon infection in turkeys." The award is sponsored by the Phipps and Bird Company, Richmond, Va.

PAUL F. RUSSELL, chief malaria consultant for the Rockefeller Foundation, has received the Darling Foundation prize for "outstanding achievements in the control of malaria." The presentation was made in Geneva, Switzerland, by Sabih Hassan al-Wahbi of Iraq, president of the World Health Assembly.

ROBERT L. FRENCH, research psychologist for the Air Research and Development Command, has been appointed technical director of the Operator Laboratory belonging to ARDC's Air Force Personnel and Training Research Center, Lackland Air Force Base, Texas.

RICHARD A. GOFF has replaced J. TEAGUE SELF as chairman of the department of zoology at the University of Oklahoma in accordance with the university's policy of rotating departmental chairmanships. Self had served as chairman for the past 12 years because he had been reappointed to serve two extra terms.

JOHN P. NASH, for the past 7 years research professor of applied mathematics at the University of Illinois, has been appointed manager of the information processing division of Lockheed Missile Systems division's research and development branch. Nash, who has offices at the missile division's research and development center in Palo Alto, Calif., will supervise the activities of the mathematics and computer services department.

JOHN J. SHEININ, president of Chicago Medical School, was one of several Americans to receive the Horatio Alger award for 1957. The award was established several years ago by the American Schools and College Association as an effort to combat a trend of thought that equal opportunity was a thing of the past.

Each year the association has awarded medals to six or seven people whose careers typify the results of individual initiative, hard work, honesty, and adherence to traditional ideals. Hundreds of names of business and professional leaders from all walks of life are submitted to the nominating committee. After screening, some 18 or 20 of these names are submitted to about 3000 campus leaders in more than 500 colleges and universities. These people, by their votes, select those whose careers they consider best reflect the spirit of achievement in spite of obstacles.

JOHN H. PETERS, clinical associate professor of medicine at Emory University, has been appointed assistant medical director for research for the American Heart Association. He will be responsible for administering the national research support program conducted by the association and its affiliates.

UGO FANO, chief of the nuclear physics section of the National Bureau of Standards, has been awarded the Department of Commerce gold medal for exceptional service, the department's highest employee honor. This award recognizes his "outstanding scientific accomplishment in the development of radiation theory." Fano is a specialist in the penetration and diffusion of radiation through matter, and his theories are widely used in connection with nuclear reactor shielding problems. At present he is on leave from the bureau, on a Rockefeller public service award, to write a book on quantum physics for nonphysicists.

GEORG VON BÉKÉSY, senior research fellow in psychophysics at the Psycho-Acoustic Laboratory, Harvard University, has received the 1957 gold medal of the American Otological Society for his contributions to the progress of otology.

JEROME HUNSAKER of Boston, Mass., has received the gold medal of the Royal Aeronautical Society (London). He was cited for "his contributions to aeronautical research and education, including his inspired chairmanship of the National Advisory Committee for Aeronautics, whose work has so greatly benefited aeronautical activities everywhere."

B. D. THOMAS, director of the Battelle Institute, Columbus, Ohio, has been awarded an honorary degree of doctor of engineering by the Michigan College of Mining and Technology (Houghton, Mich.) "in recognition of his high attainments in engineering." The degree was presented on 10 May on the occasion of the inauguration of J. R. VAN PELT as sixth president of the college. Thomas was principal speaker at the inauguration.

JOHN J. BITTNER, director of the University of Minnesota's division of cancer biology, will receive the honorary degree of doctor of medicine and surgery from the University of Perugia, Italy, on 28 July during the second International Symposium on Mammary Cancer.

ULF GRENANDER of the University of Stockholm will fill the newly established chair of mathematical statistics and probability at Brown University. He will develop courses, teach, and direct research when he takes up his duties on 1 Sept.

ARTHUR C. TOTTEN, chairman of the department of orthodontics of the Columbia University Faculty of Medicine, was honored recently at a testimonial dinner. He will retire at the end of the current term after 28 years of service. He plans to continue in private practice.

Recent Deaths

HAVEN EMERSON, New York, N.Y.; 82; public health physician, former Health Commissioner of New York City and founder of the New York Heart Association; 21 May.

HAROLD M. HIPSH, University Park, Pa.; 34; head of the department of aeronautical engineering at Pennsylvania State University; 23 May.

MAURICE J. LEWI, New York, N.Y.; 99; president of the New York College of Podiatry and early campaigner for recognition of podiatry as a branch of the medical profession; 27 May.

HENRY H. PARKE, Sycamore, Ill.; 81; at one time professor at West Virginia State College of agriculture and assistant state director of agriculture for Illinois, a founder of the American Farm Bureau Federation and the National Live Stock Producers Association; 26 May.

ROY W. SCOTT, Cleveland, Ohio; 69; professor of medicine at Western Reserve University School of Medicine, director of City Hospital's department of medicine, and former president of the American Heart Association; 25 May.

Reports

Marine Fungus Infecting Eggs and Embryos of Urosalpinx cinerea

This paper reports a fungus infestation of ova within the egg cases of the marine gastropod *Urosalpinx cinerea* (Say), the common oyster drill (*1*). This observation is important since it offers a possible biological control measure for this snail, which is one of the most destructive predators of young oysters. *Urosalpinx cinerea* is currently being studied by the U.S. Fish and Wildlife Service and other groups in an effort to develop methods for controlling its predation. This fungus is one of the few natural controlling factors known for this gastropod.

Fungus infestation in drill egg cases was first observed in cases taken from our outdoor tidal tanks, in which oyster drills are kept for laboratory study. Figure 1 shows an egg case, with its outer membrane removed, containing four dense masses which were once healthy ova and now are infected with fungus growth.

This fungus was isolated from the infested cases and was cultured by H. S. Vishniac (*2*), who thinks that it is a new form resembling *Sirolpidium zoophthorum*. She believes that this fungus belongs to the order Lagenidaiales and resembles the Sirolpidiaceae but lacks the septa which characterize this family, as defined by Sparrow (*3*). Because the fungus also resembles *Plectospira dubia* (Atkins), a marine fungus capable of infecting crustacean eggs, a pure culture of our fungus was sent to D. Atkins (*4*). She was successful in infecting the eggs of the oyster crab, *Pinnotheres*, with our isolate but is of the opinion that it is not the same as *P. dubia*.

Preliminary experiments conducted with a culture isolate demonstrated that this fungus will infect ova within the egg cases of *U. cinerea* in sterilized sea water, at 20°C, with a salinity of 21 parts per thousand. Moreover, ova do not have to be moribund for the infestation to develop. In one experiment, a flask containing 200 ml of sterile sea water and 20 washed egg cases containing ova and early gastrulae was inoculated with 3 ml of the cultured isolate. One hundred-percent infection occurred within 24 days, although the controls had developed from ova to protoconchs with no infestation.

In a similar experiment, 12 egg cases, of which four contained ova, four, veliger larvae, and four, protoconchs, were used. At the end of 28 days the four egg cases which initially contained protoconchs had released them; the veliger larvae developed to protoconchs; but the egg cases that contained ova were infected and did not develop. Normal development, with no infections, occurred in the control.

In early experiments, in which infected egg cases were used as an inoculum, only egg cases that contained ova through veliger stages were infected, not the older egg cases that contained protoconchs. Hence, infection appears to be confined to the ova and early developing stages and, in this respect, resembles the infecting behavior of *P. dubia* on crustacean eggs, inasmuch as *P. dubia* is likewise less pathogenic for the prezoeal and zoeal stages than it is in the early stages of the egg development (*5*).

Biotic control of the drill by using a trematode parasite which causes castration in snails has been suggested by Cole (*6*). The only other known biotic factor which might be considered as a means of control is a tube-dwelling amphipod, which was found to form mud tubes in drill egg cases and presumably destroys the ova of the drills on the West Coast (*6*). Hence, the fungus infestation here described presents another biotic factor which may be considered for control of *U. cinerea*. However, the practicability of control by the use of a fungus is doubtful, since any control measures in the field would demand the creation of environmental conditions conducive to infestation and dissemination. On the other hand, if this fungus can be carried and spread by the drills themselves, it may offer a specific, natural infecting agent capable of reducing efficiently the population density of the oyster drill.

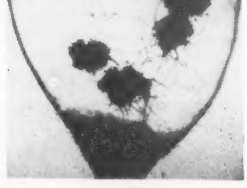

Fig. 1. An egg case of *Urosalpinx cinerea* with its outer membrane removed to show four dense masses of fungus-infested ova (×10).

A. E. GANAROS

U.S. Fish and Wildlife Service, Milford, Connecticut

References and Notes

1. I wish to thank V. L. Loosanoff, for his assistance in pursuing this problem, and C. A. Nomejko, for preparing the photomicrograph. I also wish to thank H. S. Vishniac, for preparing the fungus isolate, and D. Atkins, for allowing me to refer to her correspondence with Vishniac.
2. H. S. Vishniac, department of microbiology, Yale University, New Haven, Conn.
3. F. K. Sparrow (Univ. of Michigan Press, Ann Arbor, 1943), p. 785.
4. D. Atkins, Plymouth Marine Laboratory, Plymouth, England.
5. D. Atkins, *J. Marine Biol. Assoc. United Kingdom* 33, 721 (1954).
6. M. R. Carriker, *Special Science Rept. Fisheries* No. 148 (1955).

4 April 1957

Regulation of Liver Cholesterol Synthesis by Lymph Cholesterol

Very little is known about the homeostatic mechanism(s) regulating the blood and tissue cholesterol levels in the animal body. It has been reported that the endogenous synthesis of cholesterol is, in part, regulated by the intake of dietary sterol. In the dog and rat who have previously been fed cholesterol in their diet, there is a depression of liver cholesterol synthesis, both *in vivo* and *in vitro* (*1*). In addition, fasting has been shown to reduce markedly the rate of cholesterol synthesis in the rat (*2*).

Of particular interest to the atherosclerosis problem is the endogenous synthesis of cholesterol and its reabsorption. It has been suggested, on the basis of recent findings (*3*), that reduction of endogenous synthesis and also of reabsorption of endogenous cholesterol may lower the cholesterol level in the blood and tissues. In connection with studies on tissue cholesterol and cholesterol ester synthesis being carried out in our laboratories, an interesting observation was made on the effect of removal of

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endogenous cholesterol on cholesterol synthesis. This report describes these findings (*4*).

Rats with a thoracic lymph fistula were prepared and given saline to drink. Twenty-four hours after the operation, the lymph-fistula animals and normal fasted rats were given intraperitoneally a tracer dose of 30 μc of 1-C^{14}-acetate. The animals were sacrificed at 1 hour, and the liver and blood were removed. The total cholesterol was isolated by extraction, hydrolysis, and digitonin precipitation (*5*). The digitonides were plated and C^{14} activity was determined in a windowless gas flow counter and corrected for self-absorption.

The results, expressed as specific activity of the isolated cholesterol, are shown in Table 1. There was an eightfold increase in the specific activity of the liver cholesterol of the lymph-fistula rat over that of the normal rat. In the plasma, the specific activity of the cholesterol of the lymph-fistula rat was approximately 13 times that of the normal rat. In addition, there was no significant change in the total cholesterol content of the liver and plasma in the lymph-fistula animal.

The amount of cholesterol present in a 24-hour sample of lymph from a fasting rat is 8 to 10 mg. This represents sterol derived from the hepatic lymph and from reabsorption of cholesterol secreted in the bile and from the intestinal mucosa. It appears that the removal of this amount of endogenous cholesterol (8 to 10 mg) during a 24-hour fast leads to a pronounced increase in the rate of cholesterol synthesis in the liver. Moreover, the ratio of the specific activity of the plasma cholesterol to that of the liver cholesterol in the two types of animals suggests that there is a more rapid release to the plasma of newly synthesized cholesterol in the lymph-fistula animals.

These findings provide further evidence that the homeostatic control of cholesterol synthesis is sensitive to fluctuations in the cholesterol supply. Exogenous cholesterol depresses synthesis; in the present experiments, the "bleeding out" of 8 to 10 mg of endogenous cholesterol by way of the lymph fistula produced a marked increase in synthesis. Since exogenous cholesterol and a part of the endogenous supply of cholesterol enter the plasma by way of the thoracic duct, a major factor controlling the rate of cholesterol synthesis in the liver may be the amount of cholesterol entering the plasma by this lymph route. These experiments also pose a question whether the removal of endogenous cholesterol would be effective in lowering the levels of blood and tissue cholesterol.

Table 1. Liver cholesterol synthesis in 1 hour from 1-C^{14}-acetate in normal and lymph-fistula rats. There were four animals in each group.

Group	Specific activity (count/min mg of cholesterol)		Total concn. of cholesterol	
	Liver	Plasma	Liver (%)	Plasma (mg %)
Normal	359 ± 142	128*	0.219	58
Lymph fistula	2935 ± 293	1627 ± 173	0.212	54

* Plasma was pooled.

LEON SWELL, E. C. TROUT, JR., HENRY FIELD, JR., C. R. TREADWELL
Veterans Administration Center, Martinsburg, West Virginia, and *Department of Biochemistry, George Washington University School of Medicine, Washington, D.C.*

References and Notes

1. G. M. Tomkins, H. Sheppard, I. L. Chaikoff, *J. Biol. Chem.* 201, 137 (1953); R. G. Gould and C. B. Taylor, *Federation Proc.* 9, 179 (1950).
2. J. T. Van Bruggen *et al., J. Biol. Chem.* 196, 389 (1952).
3. D. Steinberg and D. S. Fredrickson, *Proc. Soc. Exptl. Biol. Med.* 90, 232 (1955); H. H. Hernandez *et al., Proc. Soc. Exptl. Biol. Med.* 83, 498 (1953).
4. This work was supported in part by research grants from the American Heart Association and the National Institutes of Health (H-1897 and H-2746). A paper describing our more extensive findings is in preparation.
5. A procedure for a refined gravimetric sterol method was kindly furnished by W. M. Sperry.

4 March 1957

Histochemical Demonstration of Reactivation of Acetylcholinesterase in vivo

Pyridine-2-aldoxime methiodide (2-PAM) and certain other oxime and hydroxamic acid derivatives can reactivate acetylcholinesterase *in vitro* following its inactivation by diisopropylfluorophosphate (DFP) and other irreversible alkylphosphate anticholinesterase agents (*1, 2*). The oximes can also protect animals against the lethal effects of the alkylphosphate anticholinesterases and reverse their neuromuscular blocking action (*3–6*). Although reported findings suggest that the mechanism of the protective action *in vivo* is dependent at least in part on reactivation of acetylcholinesterase, evidence for this has been found only with diaphragmatic muscle (*7*). An alternative explanation is that the protective effect of 2-PAM and similar agents may be due largely to direct combination between the oxime and the anticholinesterase agent in the body before the latter has reacted with the enzyme (*2, 8*), since in most studies the oxime has been injected intraperitoneally prior to or shortly after subcutaneous injection of the anticholinesterase agent (*3, 5*).

Recent work has indicated that the total acetylcholinesterase of neurons may consist of "functional" acetylcholinesterase, external to a lipoid-like membrane, and internal or "reserve" acetylcholinesterase; the latter may represent more recently synthesized enzyme which is stored within the endoplasmic reticulum (*9*). The pharmacological actions of anticholinesterase agents are probably due to inactivation of the former (*10*). If this represents only a small portion of the total acetylcholinesterase, its inactivation and subsequent reactivation might not be detectable by usual homogenate techniques. Furthermore, only limited quantities of quaternary agents, such as 2-PAM, might penetrate the blood-brain barrier and have access to the central nervous system.

In order to determine whether 2-PAM can reactivate acetylcholinesterase of nervous tissue and skeletal muscle *in vivo*, the following study was undertaken (*11*). Cats were anesthetized with sodium pentobarbital (30 mg/kg, intraperitoneally) and given atropine sulfate (3 mg/kg, intraperitoneally) and 20 μmole (3.68 mg) of diisopropylfluorophosphate per kilogram, (intravenously) (freshly diluted from a 0.1*M* stock solution in anhydrous propylene glycol). Four cats served as diisopropylfluorophosphate controls. Six received intravenous injections of 2-PAM at the doses and time intervals indicated in Table 1. After the cats had been sacrificed by intravenous administration of air, the stellate and ciliary ganglia and a portion of intercostal muscle were removed and sectioned immediately at 10 μ (ganglia) or 20 μ (muscle) on the freezing microtome. Sections were placed on slides and incubated in acetylthiocholine medium for 5, 10, 20, 40, and 80 minutes, after which they were developed with $(NH_4)_2S$, gold-toned, dehydrated, and mounted, (*12*). Staining was compared

Table 1. Schedule of intravenous administration of 2-PAM and sacrifice of anesthetized cats following intravenous administration of diisopropylfluorophosphate (DFP) (20 μmole/kg).

Cat No.	2-PAM (μmole/kg)	Time of administration after DFP (min)	Time of sacrifice after DFP (min)
1			35
2			35
3			78
4			79
5	20	5	35
6	40	5	35
7	20	20	35
8	40	20	35
9	40	63	78
10	40	64	79

with that of similarly treated control sections from cats which had received no diisopropylfluorophosphate or 2-PAM. Typical results are shown in the photomicrographs in Fig. 1.

In ganglia from control animals, staining for acetylcholinesterase is intense in the cell membranes and cytoplasm of the cholinergic neurons (ciliary ganglion) and considerably lighter in adrenergic neurons (majority in the stellate ganglion). Heavy staining for the enzyme is also seen in the terminations of the cholinergic preganglionic fibers, which are represented in the stellate ganglion chiefly by the protoplasmic tracts. Faint staining for nonspecific cholinesterase can be seen in the glial cells of both ganglia. In the intercostal muscle, acetylcholinesterase activity is concentrated in the subneural apparatus of the motor endplates.

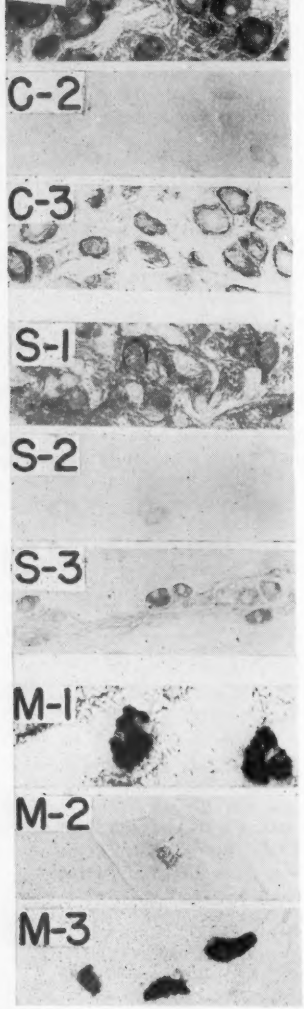

Fig. 1. Sections of ciliary ganglion (*C*), stellate ganglion (*S*) and intercostal motor endplates (*M*) of cats, stained for acetylcholinesterase. 1, Control; 2, diisopropylfluorophosphate (20 μmole/kg) 79 min prior to sacrifice; 3, diisopropylfluorophosphate 79 min and 2-PAM (40 μmole/kg) 15 min prior to sacrifice. Ganglia were incubated 80 min, magnification × 120; endplates were incubated 20 min, magnification × 350.

The acetylcholinesterase of the ganglia of the diisopropylfluorophosphate controls sacrificed at 35 minutes was practically completely inactivated. In the two controls sacrificed at approximately 80 minutes, there was faint staining of the cytoplasm of the cholinergic neurons, suggesting the synthesis of new acetylcholinesterase. This is in keeping with the aforementioned conclusion that synthesis of the enzyme may occur within the endoplasmic reticulum (*9*). Marked reduction occurred in the acetylcholinesterase activity of the motor endplates, which showed, however, considerable variation in intensity.

Findings in all six cats which received diisopropylfluorophosphate followed by 2-PAM were practically identical, despite the differences in doses and time intervals. The cholinergic neurons of the ciliary ganglia showed distinct peripheral staining, and faint but definite staining within the cytoplasm. The same was true of the cholinergic neurons of the stellate ganglion; in this tissue, staining could be seen also in the protoplasmic tracts. Staining of the motor endplates varied, but the average intensity was considerably greater than that of the controls.

When diisopropylfluorophosphate is injected intravenously, most of the agent probably reacts with esterases and other constituents of the tissues within a few minutes; after an hour, it is highly unlikely that any uncombined compound is present (*13*). Therefore, these results appear to demonstrate conclusively that 2-PAM can reactivate acetylcholinesterase of neurons and motor endplates *in vivo* after its inactivation by diisopropylfluorophosphate.

GEORGE B. KOELLE

Department of Physiology and Pharmacology, Graduate School of Medicine, University of Pennsylvania, Philadelphia

References and Notes

1. I. B. Wilson and E. K. Meislich, *J. Am. Chem. Soc.* 75, 4628 (1953); I. B. Wilson, S. Ginsburg, E. K. Meislich, *ibid.* 77, 4286 (1955); I. B. Wilson and S. Ginsburg, *Biochim. et Biophys. Acta* 18, 168 (1955); A. F. Childs *et al.*, *Brit. J. Pharmacol.* 10, 462 (1955).
2. B. J. Jandorf, E. A. Crowell, A. P. Levin, *Federation Proc.* 14, 231 (1955).
3. H. Kewitz, I. B. Wilson, D. Nachmansohn, *Arch. Biochem. and Biophys.* 64, 456 (1956).
4. R. Holmes and E. L. Robins, *Brit. J. Pharmacol.* 10, 490 (1955).
5. B. M. Askew, *ibid.* 11, 417 (1956).
6. J. H. Wills *et al.*, *Science* 125, 743 (1957).
7. H. Kewitz, *Arch. Biochem. and Biophys.* 66, 263 (1957); H. Kewitz and D. Nachmansohn, *ibid.* 66, 271 (1957).
8. J. Wagner-Jauregg and B. E. Hackley, Jr., *J. Am. Chem. Soc.* 75, 2125 (1953); B. E. Hackley *et al.*, *ibid.* 77, 3651 (1955).
9. G. B. Koelle and E. W. Steiner, *J. Pharmacol. Exptl. Therap.* 118, 420 (1956).
10. G. B. Koelle, *ibid.*, in press.
11. This investigation was supported by research grant B-282 (C4) from the National Institute of Neurological Diseases and Blindness, National Institutes of Health, U.S. Public Health Service. Pyridine-2-aldoxime methiodide was kindly supplied by J. Henry Wills, and diisopropylfluorophosphate by William C. Summerson, Army Chemical Center, Md. Photomicrographs were taken by E. W. Glifort. The valuable technical assistance of Priscilla Smart is gratefully acknowledged.
12. G. B. Koelle, *J. Pharmacol. Exptl. Therap.* 103, 153 (1951).
13. B. J. Jandorf and P. D. McNamara, *ibid.* 98, 77 (1950).

1 March 1957

New Mutation in Polioviruses

During the last several years our knowledge of the mutation of polioviruses has been much increased through studies in various *in vitro* systems. Mutants of reduced virulence for monkeys have been discovered (*1*). With regards the size of plaque on monolayers of monkey kidney cells, Dulbecco and Vogt (*2*) have obtained an *r* (rapid) mutant of Brunhilde, and Dubes (*3*) has isolated slow Mahoney, a genetic variant of Mahoney that produces relatively tiny plaques. Dubes (*4*) has also reported on the cold-adapted variants of polioviruses. Heat-resistant variants of polioviruses were also isolated (*5*).

It has been shown (*6*) that spontaneously occurring neutralizing substances for three types of poliovirus can be found in normal adult bovine serums. Although the data thus far accumulated indicate apparently the possible identity of the neutralizing substances with the antibody, it must be admitted that the evidences are not yet conclusive enough, and further experimental work is required before this can be accepted as proved. Accordingly, in this report we refer to these substances as normal bovine serum (NBS) inhibitors for the sake of brevity.

In the work reported here (*7*), mutants of the poliovirus strains, Mahoney and MEF-1, "resistant" to NBS inhibitors, have been obtained readily through serial passages of the parental viruses in HeLa cell cultures with a medium containing 20 to 40 percent inhibitory normal bovine serum. Our strain of HeLa cells has been propagated quite satisfactorily during the last 15 months in medium YLA (Earle, 0.5 percent lactalbumin hydrolyzate and 0.1 percent Difco yeast extract) (*8*), supplemented with only 20 percent normal bovine serum.

A simple method was devised that can

be used both for the demonstration of NBS inhibitors in bovine serums and for the detection of mutants of polioviruses resistant to NBS inhibitors. When monolayers of either HeLa cells or monkey kidney cells that had been inoculated with parental polioviruses were overlayered with YLA agar containing 10 to 20 percent inhibitory normal bovine serum, only small plaques (usually 0.5 to 1.5 mm) were produced 4 to 5 days after seeding. In contrast, larger plaques (up to 8 to 10 mm) were formed on control plates that were overlayered with agar containing 10 percent noninhibitory horse or calf serum. Furthermore, it was found that plaques produced by the resistant mutants are definitely larger than those produced by the parental polioviruses on inhibitory agar plates and approach the plaque sizes of the latter on the control plates. After the large mutant plaques have been replated on inhibitory agar plates, clones of the mutant virus can be readily obtained.

Both Mahoney and MEF-I strains were first twice plaque-purified on HeLa cell monolayers, and respective stocks, grown on HeLa cell cultures, were used to initiate serial passages. A bottle culture of HeLa cells (5 to 8×10^6 cells) with 9 ml of medium YLA supplemented with 40 percent inhibitory NBS-120 was inoculated with 1 ml of undiluted Mahoney stock (10^8 pfu/ml) and examined daily for cytopathogenic action. As soon as cellular degeneration was complete, culture fluid was harvested and 1 ml of the harvested fluid was inoculated again into a new HeLa cell bottle culture containing 40 percent NBS-120. A resistant mutant was obtained from the seventh passage of the series of serial passages.

After the mutant had been plaque-purified on HeLa cell monolayers, the plaque sizes of the mutant (Pl-289) and those of the parental Mahoney were compared on HeLa cell monolayers (Table 1.) It is clear that plaques of the mutant (Pl-289) are definitely larger than those of the original Mahoney on HeLa cell monolayers with 20 percent NBS-120 agar overlay and that the plaques show a distribution essentially similar to that of parental Mahoney on control plates.

In another experiment, resistant mutants were detected even after single passage of parental MEF-1 virus in HeLa cell bottle culture in the presence of 40 percent strongly inhibitory NBS-70. In this instance, cellular destruction was complete only 7 to 9 days after inoculation of 1 ml of undiluted MEF-1 stock. Plaque sizes of a mutant of MEF-1 (Pl-91) thus obtained are compared with those of parental MEF-1 on monolayers of monkey kidney cells in Fig. 1. It is clear that the mutant (Pl-91) produces larger plaques than those of the original MEF-1 on monkey kidney monolayers with NBS-70 agar overlay.

These mutants of both types of poliovirus isolated from different series of serial passages have been studied with respect to their sensitivity to NBS inhibitors. Undiluted normal bovine serum used for respective serial passages and virus (10^5 pfu/ml) were mixed and incubated at 37°C. At various subsequent times, a sample of the mixture was further diluted and assayed for active virus by the plaque method (*9*) on HeLa cell monolayers to determine the kinetic curve of inactivation (*10*) of the original and mutant viruses. In each case, it was clearly observed that the mutant viruses were inactivated definitely slower and to a lesser extent than the respective original viruses. Therefore it may be concluded at least that mutation to resistance to NBS inhibitors is involved in the formation of larger plaques on the NBS inhibitor plates, although it does not exclude the possibility that other types of mutation may also be involved. In contrast, since no apparent difference could be demonstrated between the kinetic curves of neutralization (*10*) of the original viruses and respective mutants with homologous antiserum, it is clear that the mutants are immunologically identical with the respective original viruses.

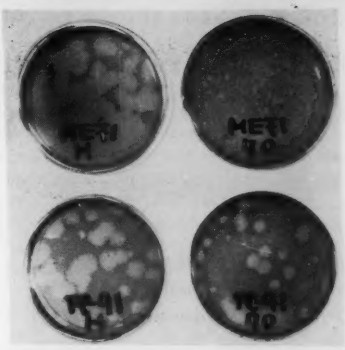

Fig. 1. Comparison of plaque sizes of plaque-purified MEF-1 stock and its resistant mutant (Pl-91), isolated and twice plaque-purified after single passage of parental MEF-1 in HeLa cell bottle culture with medium containing 40 percent NBS-70, on monolayers of monkey kidney cells. *H* and 70, agar overlay containing 10 percent horse serum and 20 percent NBS-70, respectively. The photograph was taken 3 days after inoculation (approximately one-half natural size).

The resistant mutants have been compared with the original viruses in virulence for mice by both the intracerebral and intraspinal routes of inoculation. The data available at this time show that the resistant mutants of both Mahoney and MEF-1 do not differ in virulence in mice from their respective progenitors. The mutants were found to be stable through ten rapid serial passages in tissue cultures of HeLa, monkey kidney cells, and embryonic human skin muscle in the absence of NBS inhibitors.

Table 1. Distribution of plaque sizes of parental Mahoney virus and its mutant "resistant" to normal bovine serum (NBS) inhibitor on monolayers of HeLa cells.

Virus		Content of agar overlay	Frequency distribution of plaque sizes (5%)*						
			Plaque diameter (mm)						
Strain	Diln.		< 0.5	1	2	3	4	5	6
Mahoney, plaque-purified wild type	10^{-5}	10% horse serum	7.6	18.6	15.7	32.0	15.7	7.9	2.4
Mahoney, plaque-purified wild type	10^{-5}	20% NBS-120	100	0	0	0	0	0	0
Pl-289, plaque-purified Mahoney mutant†	(¼) 10^{-4}	10% horse serum	19.3	30.0	37.9	9.3	2.9	0.7	0
Pl-289, plaque-purified Mahoney mutant†	(¼) 10^{-4}	20% NBS-120	12.2	25.2	18.3	25.2	13.0	4.6	1.5

* After 4 days' incubation at 37°C, 200 to 400 plaques were counted. All the determinations were made on the same lot of HeLa cell monolayers.
† Isolated from the seventh passage in HeLa cell bottle culture with a medium YLA containing 40 percent inhibitory NBS-120.

NOBUYUKI TAKEMORI, SHIGEKO NOMURA
MINORU NAKANO, YUTAKA MORIOKA
MITSUO HENMI, MASAMI KITAOKA
National Institute of Health, Shinagawa-ku, Tokyo, Japan

References and Notes

1. J. F. Enders, T. H. Weller, F. C. Robbins, *Federation Proc.* 11, 467 (1952); A. B. Sabin, W. A. Hennessen, J. Winsser, *J. Exptl. Med.* 99, 551 (1954); C. P. Li, M. Scheaffer, D. B. Nelson, *Ann. N.Y. Acad. Sci.* 61, 902 (1955); J. L. Melnick, *Federation Proc.* 13, 505 (1954).
2. R. Dulbecco and M. Vogt, *Ann. N.Y. Acad. Sci.* 61, 790 (1955).
3. G. R. Dubes, *Virology* 2, 284 (1956).
4. ——— and M. Chapin, *Science* 124, 586 (1956).
5. M. Vogt and R. Dulbecco, *2nd Seminar on Quant. Animal Virol.* (1955); N. T. Stanley *et al., Nature* 178, 413 (1956).
6. A. B. Sabin and A. H. Fieldsteel, *6th Intern. Congr. Microbiol.* 2, 373 (1953); P. Bartell

and M. Klein, *Proc. Soc. Exptl. Biol. Med.* **90**, 597 (1955).
7. This work was aided by a grant from the Asahi Shinbun. A full description of the details of these studies is in preparation.
8. R. Dulbecco and M. Vogt, personal communication (1955).
9. ———, *J. Exptl. Med.* **99**, 167 (1954).
10. ——— and A. G. R. Strickland, *Virology* **2**, 162 (1956).

4 March 1957

Inability of Nitrate to Serve as a Terminal Oxidant for Hydrocarbons

Denitrifying or nitrate-reducing bacteria are capable of growing aerobically in the absence of nitrate. All compounds which serve aerobically as energy sources for these organisms will serve in the same capacity anaerobically if nitrate is present as the electron acceptor. The only known exception to this rule is the inability of denitrifying bacteria to utilize aromatic acids anaerobically in the presence of nitrate (*1*).

During a study of the mechanisms of microbial hydrocarbon oxidation, attempts were made to isolate nitrate-reducing bacteria by the technique of van Iterson (*2*), with various straight chain, aliphatic hydrocarbons as the oxidizable substrate (*3*). Such isolation procedures were uniformly unsuccessful. The same technique, on the other hand, when citrate and ethanol were used as sources of energy, yielded large numbers of denitrifiers from soil samples. Numerous cultures conforming to the description of *Pseudomonas stutzeri* (*4*) were isolated in pure culture.

To ascertain whether cultures isolated in this manner would oxidize hydrocarbons anaerobically in the presence of nitrate, the technique of Allen and van Niel was employed (*5*). Essentially, the technique measures substrate oxidation by a conventional manometric determination of the nitrate reduction product (nitrogen). Hydrocarbons were supplied to washed, resting cells of organisms grown anaerobically in yeast extract-peptone-nitrate broth as a 1-percent (volume by volume) emulsion in water. Homologous oxygen-containing derivatives were similarly dispersed and tested. Commercially available hydrocarbons appeared to be oxidized to a small but significant extent, but, when highly purified hydrocarbons (*6*) from the American Petroleum Institute were used, no oxidation was detected under anaerobic conditions with nitrate present (Fig. 1). All the homologous oxygen-containing compounds tested were readily oxidized anaerobically. No particular significance should be attached to the rates of oxidation, since they probably depend, in part, on degree of dispersion and surface area of substrate available.

The data present another exception to the general rule concerning oxidative abilities of nitrate-reducing bacteria. A possible explanation for the failure of aromatic acids to function as oxidizable substrates for denitrifying organisms anaerobically is found in the suggestion of Stanier (*7*) and Parr *et al.* (*8*) that the primary attack on the aromatic nucleus by bacterial enzymes involves the simultaneous introduction of two hydroxyl groups—that is, a peroxidation. Peroxidations rarely occur in the absence of oxygen, since molecular oxygen is generally implicated directly in the formation of the peroxide involved. Alternatively, the primary enzymatic attack on the paraffin molecule may involve the direct participation of oxygen in the reaction, as is the case in pyrocatechase (*9*). Hayaishi and coworkers (*10*) have recently shown that two types of these "oxygenases" exist; one type (phenolytic oxidases) adds both atoms of an oxygen molecule to the substrate, while the second type splits the oxygen molecule, reducing one to water and adding the other to the substrate. *P. stutzeri* will grow at the expense of benzoic acid aerobically but not in the absence of oxygen, even if nitrate is supplied (*5*).

A parallel situation exists with the hydrocarbons. Strains of *P. stutzeri* that are unable to oxidize hydrocarbons anaerobically readily oxidize paraffins and olefins aerobically (Fig. 1, right). Aerobically grown cells did not oxidize hydrocarbons anaerobically. It is interesting to note that the "aerobic" oxidation of both paraffins and olefins among those tested (C_{12}, C_{14}, and C_{16}) occurred without detectable induction period, even though hydrocarbon was absent from the growth medium.

These observations lend some credence to the suggestion (*11*) that peroxidation or some other oxygen-requiring mechanism is the first step in the biological oxidation of hydrocarbons and, together with the findings of Updegraff and Wren (*12*), suggests that there are probably very few anaerobic oxidations of paraffins (with the possible exception of methane) by either nitrate-reducing or sulfate-reducing bacteria. Once the hydrocarbon structure has been breached by introduction of oxygen, by means of peroxidation or oxygenase action, oxidation at the expense of nitrate reduction and, presumably, sulfate reduction (by *Desulfvibrio* species) occurs readily.

It is not suggested here that the oxygen-containing compounds tested are the immediate intermediates in the oxidation of paraffins. Intermediates isolated during the course of paraffin oxidation are being characterized and will be described later.

ROBERT W. HANSEN*
R. E. KALLIO

College of Medicine,
State University of Iowa, Iowa City

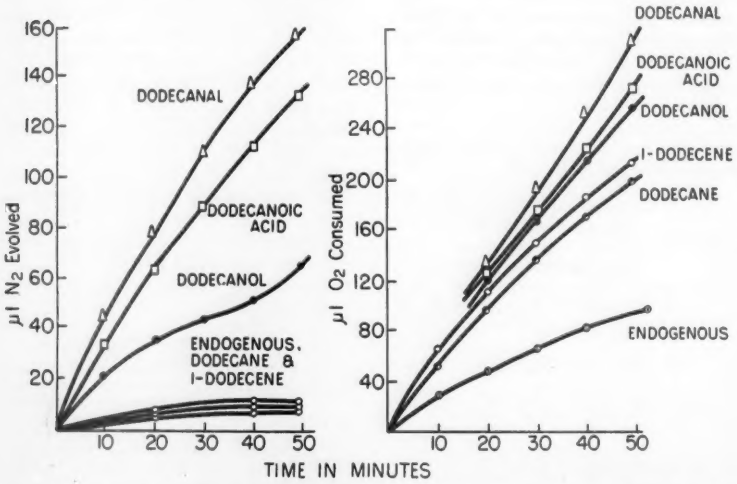

Fig. 1. Oxidations of dodecane, 1-dodecene, and corresponding oxygen-containing derivatives by resting cells of *P. stutzeri*, grown in yeast extract-peptone-nitrate medium. Each vessel contained 8 mg (dry weight) of cells, 0.5 ml of 1 percent (volume by volume) suspension of substrate, and 0.8 ml of 0.02*M* phosphate buffer (*p*H 7.2). Each flask contained in addition, 20 μmole of nitrate. Incubation was at 30°C. N_2 evolution was measured under anaerobiosis; both sets of data were derived from the same cell suspension.

References and Notes

1. G. van Iterson, Jr., *Chem. Weekblad* **1**, 691 (1904).
2. ———, *Proc. Koninkl. Akad. Wetenschap. Amsterdam* **5**, 148 (1902).
3. This study was supported in part by a grant from the Petroleum Research Fund of the American Chemical Society.
4. C. B. van Niel and M. B. Allen, *J. Bacteriol.* **64**, 413 (1952).
5. M. B. Allen and C. B. van Niel, *ibid.* **64**, 397 (1952).
6. American Petroleum Institute standard samples. API dodecane contains 0.031 ± 0.025 mole percent of impurity; API 1-dodecene

contains 0.13 ± 0.07 mole percent of impurity.
7. R. Y. Stanier, *J. Bacteriol.* **55**, 477 (1948); *Bacteriol. Revs.* **14**, 179 (1950).
8. W. H. Parr, R. A. Evans, W. C. Evans, *Biochem. J.* **45**, xxix (1949).
9. O. Hayaishi, M. Katagiri, S. Rothberg, *J. Am. Chem. Soc.* **77**, 5450 (1955).
10. O. Hayaishi, S. Rothberg, A. H. Mehler, Abstr. of papers, Am. Chem. Soc. meeting, Atlantic City, N.J., 20 Sept. 1956, p. 530.
11. E. Beerstecher, Jr., *Petroleum Microbiology* (Elsevier, Houston, Tex., 1954).
12. D. M. Updegraff and G. B. Wren, *Applied Microbiol.* **2**, 309 (1954).
* Present address: Campbell Soup Company, Chicago, Ill.

25 March 1957

Relationship between Auxin and Membrane-Integrity in Tissue Senescence and Abscission

Previous investigations have shown that the physiological aging and abscission of fruits and foliar organs attend a drop in the auxin level of these determinant organs (*1*). This report presents some experimental evidence of the probable role of auxin in such phenomena (*2*).

Segments of commercially grown Kentucky Wonder pole beans were prepared as described by Bonner and English (*3*). From 10 to 20 segments were placed, with all, part, or none of the exocarp removed, in petri dishes on filter papers, which were kept moist with distilled water or distilled water plux auxin [indole-3-acetic acid (IAA) or naphthalene acetic acid (NAA)] at concentrations of 4 to 50 ppm. The experiments were conducted both with and without asepsis. The dishes were stored in the dark at 25°C.

At the end of 2½ to 3 days, under aseptic conditions, the segments treated with 4 ppm auxin were plump and rigid, while the controls (water-treated) were soft and flaccid. Rigidity, however, was not directly related to the amount of water absorbed, for under some conditions the auxin-treated segments took up less water than did the control segments.

Hand sections made after 2½ to 3 days revealed that, in the segments treated with auxin, the intercellular spaces were filled with air (Fig. 1); this is a normal situation, as is shown by comparison with sections of fresh, whole beans. In contrast, sections of the controls showed that their intercellular spaces were filled with liquids (Fig. 2). Thus, it appears that the role of auxin in maintaining rigidity of the bean tissue is the result of an effect on membrane permeability; the auxin functions to maintain the selective permeability of the membranes, thereby preventing the exosmosis of cellular substances into the intercellular spaces. The latter process may be visualized as causal of disturbances in equilibria, which accelerate senescence.

Subsequent to liquid-logging of the intercellular spaces, there occurred a dissociation of cells, manifested by their separating at the middle lamella and rounding-up. The possibility that pectinases may be among the cellular substances liberated into the spaces is being investigated.

With concentrations of 4, 25, and 50 ppm auxin, membrane-integrity in the bean segments was maintained for 7, 11, and 17 days, respectively. In experiments performed without asepsis, the first sign of contamination appeared after the loss of membrane-integrity. Rapid bacterial decomposition followed as a result of the favorable substratum provided by the loss of cellular substances.

Auxin was most effective in maintenance of membrane-integrity when it was applied immediately. After 24 hours of water treatment it gave partial effects, and after 48 hours, no effects. This indicates that membrane-alteration begins during 24 hours, and is irreversible after 48 hours, of water treatment.

Sections of limp, whole beans showed that the effect of auxin on membrane-integrity is unrelated to the phenomenon of water loss that occurs as beans wilt, for the intercellular spaces were filled with air, although much water had been lost.

There was a differential response of tissues of the bean segments to loss of membrane-integrity. If such differential developments were to take place in selected tissues in other material, such as the abscission zone, the following hypothesis is suggested. The cells of the abscission zone are especially sensitive to a drop in auxin level. Below a critical level, the cells in this zone lose the integrity of their membranes; this permits the displacement of cellular fluids which affect the middle lamella, causing dissociation of cells, and the leaf abscises. Following are the results of some experiments on the effects of auxin on the abscission zone in *Coleus*.

A profusely branched stock of *Coleus* was used for the experimental work (*4*). Longitudinal hand sections show that the cells of the petiole are arranged in longitudinal rows, with conspicuous and continuous intercellular spaces oriented longitudinally and extending through the abscission zone. These spaces are normally filled with air, as is evidenced by their interference with transmission of light owing to reflection phenomena (Fig. 3).

Coleus shoots were spirally debladed from nodes 1 to 6, inclusive (*5*). Within 3 days the debladed petiolar stumps at nodes 3 to 6 had abscised, while petioles at the uppermost nodes 1 and 2 were intact. Hand sections of debladed petioles from node 1 showed that the air in the intercellular spaces had been displaced by cellular fluids only in the cell layers of the abscission zone (Fig. 4). Various stages in the liquid-logging of the spaces were observed by means of fresh sections of many debladed petioles from nodes 1 and 2. At each node the opposite, nondebladed petiole served as a control. The controls always showed intact air columns through the abscission zone.

Subsequent to the loss of selective permeability of the cell membranes in the abscission zone (evidenced by liquid-logging of the spaces) there was apparent a dissociation of cells, manifested by

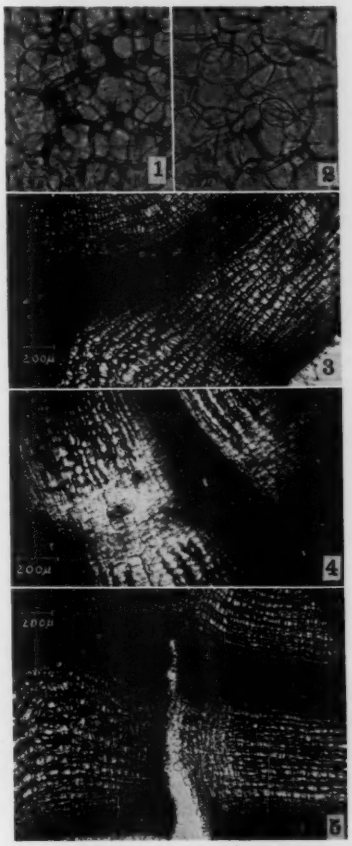

Fig. 1. Fresh section of bean segment after 3 + days of auxin treatment, showing air-filled intercellular spaces (they appear black, owing to reflection phenomena). Fig. 2. Fresh section of bean segment after 3 days of water treatment. Intercellular spaces are filled with liquid as a result of loss of membrane-integrity. Fig. 3. Longisection of control petiole (with blade intact) of *Coleus*. Note the air-filled intercellular spaces traversing abscission zone. Fig. 4. Longisection of petiolar stump (node 1), 3 days after deblading. Intercellular spaces in abscission zone are filled with liquid, owing to loss of membrane-integrity. Fig. 5. Longisection of petiolar stump (node 2), 3 days after deblading. Note centripetal progression of abscission, owing to dissolution of middle lamella.

their separating and assuming a spherical shape. This is illustrated in Fig. 5—a stage where complete dissolution of the middle lamella had occurred, resulting in the centripetal progression of abscission.

The hypothesis that auxin inhibits abscission through its effect on the maintenance of membrane-integrity was further supported by experiments in which 1 percent IAA in lanolin-water emulsion was applied distally on debladed petiolar stumps. Hand sections of these petioles, 3, 5, and 10 days after deblading, revealed a continuity of air in the intercellular spaces traversing the abscission zone.

A similar mechanism may be operative, attending a drop in auxin level, during tissue senescence in certain fleshy fruits as well as in abscission of determinant organs in other plants.

JOSEPH A. SACHER
Los Angeles State College and
Division of Biology, California Institute of Technology, Pasadena

References and Notes

1. L. C. Luckwill, *J. Hort. Sci.* **24**, 32 (1948); K. Shoji, F. T. Addicott, W. A. Swets, *Plant Physiol.* **26**, 189 (1951).
2. This investigation was supported by a summer (1956) research award from the Lalor Foundation and was conducted in Kerckhoff Biology Laboratories, California Institute of Technology, Pasadena, where I hold an appointment as research fellow. During the course of the investigation A. J. Haagen-Smit offered suggestions and encouragement, for which I express my sincere thanks.
3. J. Bonner and J. English, Jr., *Plant Physiol.* **13**, 331 (1938).
4. The *Coleus* stock was grown in Earhardt Laboratory, California Institute of Technology.
5. R. H. Wetmore and W. P. Jacobs, *Am. J. Botany* **40**, 272 (1953).

25 March 1957

Differential Responses to Population Pressures by Normal and Dwarf Lines of Maize

Dwarf or semidwarf variants in such species as sorghums, apples, beans, and peas are of economic importance. Suggestions have been made that one of the numerous, genetically different, semidwarf mutants of maize might also be useful agriculturally. The rationale has been that the shortened stalk of such dwarf types would markedly reduce the incidence of stalk breakage and root lodging which make machine harvesting difficult. Therefore, these types would be acceptable if their yield were equal to or only slightly below normal. Leng (*1*) recently reported that single crosses made from inbreds which had been converted to the recessive mutant *brachytic* 2 were satisfactory in yield.

Field observations in our laboratory of dwarf types had indicated that they might actually possess yielding ability beyond their normal counterparts. These observations motivated the start of a testing program in 1954 designed to characterize the response of both dwarf and normal types to population pressures at high levels of fertility and with adequate water available. Work during the past 3 years has shown that at least one recessive semidwarf mutant *compact* (*ct*) has a significantly different response to population pressures from the normal inbred Hy or two other semidwarf mutants *reduced* and *brachytic* 2 (*2*).

The *compact* mutant arose by spontaneous mutation in a stock of Hy2 and has previously been designated as Hy2 (*dwarf*). It has been compared for 3 years in replicated yield tests to the normal Hy inbred, for 2 years to a Hy conversion to *reduced*, and for 1 year to a Hy conversion to *brachytic* 2. Thus all types under test were inbreds which had roughly comparable genotypes except for the loci conditioning plant height. Data on grain and stover yields, leaf areas, mineral content of the leaves, flowering dates, and ear characteristics were collected for each strain at various population levels. Figure 1 shows the yield in bushels per acre at four populations for 1956, the only year in which all four genetic strains were compared. Note the attainment of a yield optimum at 26,000 plants per acre by the *compact* strain and only slight decreases in yield at the higher populations; this is in marked contrast to the other types tested. Note, too, that at 26,000 plants per acre, the *compact* strain yields more than the normal strain yields at 13,000 plants per acre. Such a superiority in yield for the *compact* strain at higher populations over the normal strain at any population tested was also noted in the 1954 and 1955 tests.

The test reported here was made with inbred material, Hy, and various semidwarf mutants inserted into a Hy background. It would be unwarranted to extrapolate from the responses of inbreds to population pressures to the responses of hybrids. Other tests have shown, however, that normal hybrids with Hy as one parent react similarly to Hy with regard to population increases. Further, *reduced* hybrids respond in much the same manner as *reduced* Hy while *brachytic* 2 hybrids are similar to *brachytic* 2 Hy.

The *compact* strain clearly has a different response to high populations from three other comparable strains carrying other genes affecting plant size. This response enables *compact* to yield slightly more at high populations than the normal type yields at any population tested. Further, inbreds and hybrids carrying the same dwarfing gene (either *rd* or *br*2) react similarly to population pressures. These findings suggest that yield increases over normal hybrids can be obtained by the use of hybrids converted to the *compact* gene. Preliminary tests of partially converted hybrids will be made in 1957 (*3*).

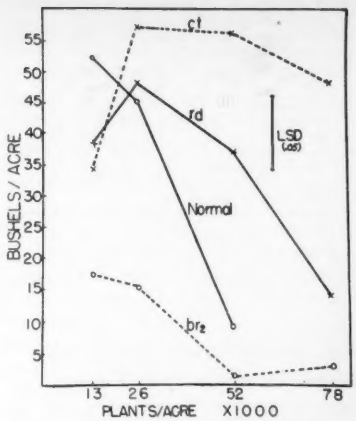

Fig. 1. Yields in bushels per acre for four inbreds which are genetically similar except for major genes that affect plant size (1956).

O. E. NELSON, JR.
A. J. OHLROGGE
Department of Botany and Plant Pathology, and *Department of Agronomy, Purdue University, Lafayette, Indiana*

References and Notes

1. E. R. Leng, *Abstr. Am. Soc. Agron.* (1956), p. 69.
2. We are indebted to W. R. Singleton for seed of the *reduced* types and to E. R. Leng for seed of the *brachytic* types.
3. This article is journal paper No. 1101 of the Purdue University Agricultural Experiment Station.

15 March 1957

Selective Blockade of Excitatory Synapses in the Cat Brain by γ-Aminobutyric Acid

γ-Aminobutyric acid (GABA) has been identified (*1*) as an active principle in the inhibitory substance (factor I) that can be extracted from the mammalian brain (*2*). Both the extract and the compound have been tested, chiefly on the crayfish stretch receptor (*1–3*), and both diminish the depolarizing electrogenesis caused by stretch of its mechano-sensitive dendrites. GABA also appears to augment the inhibitory postsynaptic potential of the receptor (*3*). On the dog brain, both "excitatory" and "inhibitory" effects by GABA and other amino acids have been reported (*4*).

The mode by which a synaptic drug exerts its overt effects in the central nervous system is often difficult to determine (*5, 6*). For example, although

strychnine and Metrazol are both classified as "stimulants of the central nervous system" (*7*), only the latter is truly a synaptic excitant (*6*). The overt excitatory activity produced by strychnine is caused by selective blockade of inhibitory synapses. Methods, developed in this laboratory, that can distinguish the modes of action of synaptic drugs have been used to analyze the effects of GABA in the mammalian central nervous system.

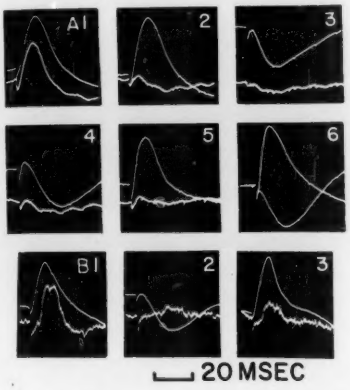

Fig. 1. Effects of GABA on postsynaptic potentials evoked in cerebral and cerebellar cortex of cat by surface electric stimuli. The stimuli were 0.1 msec square pulses, applied through a pair of closely spaced 100-μ silver wires, Teflon-insulated except at their cross sections, which rested lightly on the cortical surface. The active recording electrode was a silver ball about 1 mm distant from the stimulating electrodes. (*A*) Surface-negative responses in cerebral cortex (suprasylvian gyrus) shown on upper cathode-ray oscillograph traces: 1–5, lower trace, simultaneously registered the activity recorded with a 100-μ wire electrode, insulated except at the tip; 1 and 2, responses before application of GABA; 1, both recording electrodes on surface; 2, wire inserted 0.4 mm below the surface. In 3–5, recording conditions were as in 2; 3, reversal of surface negativity developing 20 sec after application of GABA to the region of the electrodes (3 drops, 10^{-2} w/v); 4, 30 sec later, full reversal; 5, 1 min after flushing the cortex with saline solution; 6, superimposed dendritic responses recorded from the surface before and after applying GABA, showing relative time relations. (*B*) Upper trace, from cerebral; lower trace, from cerebellar cortex, simultaneous oscillographic recordings: 1, surface-negative responses produced by a stimulus to each cortical surface; 2, topical applications of GABA (5 drops, 10^{-3} w/v) to each site reversed the response of the cerebral activity but diminished and abolished that of the cerebellar cortex. The cerebellar effect, blockade of its excitatory axodendritic synapses, developed more slowly than did the action on the cerebral cortex; 3, recovery of both cortical responses 2 min after flushing with Ringer's solution.

Injected into unanesthetized succinylcholine-paralyzed cats, even in high concentrations (100 mg/kg, intravenously, in one dose), GABA has only minimal, transient effects on responses evoked in the cerebral or cerebellar cortex by diverse pathways. When applied topically, buffered at *p*H 7.4, GABA in dilutions of 10^{-5} weight for volume exerts marked effects on evoked cortical responses. Rapid, pronounced actions occur with application of strong solutions (Fig. 1). These are quickly reversible upon flushing of the cortical surface with Ringer's solution, and the cycle may be repeated many times.

The effects of GABA differ characteristically in the cerebral and cerebellar cortex, thereby defining one mode of its action. The surface-negative postsynaptic potentials of the apical dendrites produced in the cerebral cortex by various stimuli (*6*) are reversed by GABA (Fig. 1, A1-6). The consequent surface-positivity (Fig. 1, A3, 4, 6) is almost a mirror image of the previous negativity (Fig. 1, A6). This large change in surface potentials has no correlate anywhere below the cortical surface. The reversed activity, therefore, is a "standing" potential characteristic of postsynaptic potentials (*5*), and the positivity induced by GABA represents hyperpolarizing synaptic electrogenesis of the apical dendrites.

Applied to the cerebellar cortex (Fig. 1, B1-3) GABA also eliminates the surface negative dendritic postsynaptic potentials, but does not induce positivity (Fig. 1, B2). The difference in action at the two sites is ascribable to the relative paucity of inhibitory synapses in the cerebellar cortex (*6*). It also indicates that at least one mode of action of GABA is to block, selectively, the electrogenesis of depolarizing, excitatory synapses. The reversal of potential observed in the cerebral cortex may be accounted for as the disclosure of hyperpolarizing postsynaptic potentials that are normally masked by countervailing synaptic depolarizations (*6*).

Of a number of substances tested thus far, including various amino acids, only β-alanine exerts effects similar to, but weaker than, those of GABA, a relationship that also obtains for the crayfish stretch receptor (*2*). Cytidine and uridine, which sustain electrocortical activity of the perfused brain (*8*), caused no marked effects. Therefore, these nucleosides probably act on metabolic processes of the brain, not directly on synaptic electrogenesis.

Picrotoxin, *l*-carnosine, and strychnine "antagonize" the effects of GABA but by two characteristically different modes (Fig. 2). Carnosine, the "excitin" of Hayashi (*9*), and picrotoxin are, like Metrazol, excitants of synaptic activity and thus (*5*) act as competitive antagonists of GABA. Strychnine merely eliminates the surface positivity by blocking the inhibitory synapses that remain after GABA has blocked the excitatory synapses.

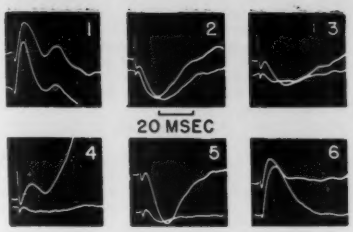

Fig. 2. Interaction of GABA with picrotoxin and strychnine. Simultaneously recorded responses to independent stimulations of homologous points of right (upper trace) and left (lower trace) anterior suprasylvian gyrus, the cerebral hemispheres being disconnected by callosal section: 1, initial dendritic postsynaptic potentials; 2, 30 sec after application of GABA (3 drops, 10^{-2} w/v) to each side. Picrotoxin (2 drops of 3×10^{-3} w/v solution) was then applied to right cortex and strychnine sulfate (2 drops of 5×10^{-3} w/v) to the left; 3, 20 sec later; 4, 1 min later, after another application of the drugs; 5, 2 min later and 30 sec after another application of GABA. Whereas the effects on the strychninized (left) cortex were minimal, marked antagonism to picrotoxin is seen; 6, 15 min after repeated washing of the cortex with Ringer's solution. Recovery of previously inactive strychninized side is the more rapid, probably denoting persistent blockade of inhibitory synapses.

The foregoing experiments demonstrate, therefore, that GABA blocks depolarizing, excitatory synaptic electrogenesis in the mammalian brain as it also blocks that of the mechanosensitive receptor (*1–3*). The tests carried out thus far do not, however, preclude the possibility that GABA may also augment inhibitory postsynaptic potentials of the brain (*10*).

DOMINICK P. PURPURA*
MARTÍN GIRADO
HARRY GRUNDFEST†
Departments of Neurological Surgery and Neurology, College of Physicians and Surgeons, Columbia University, New York

References and Notes

1. A. Bazemore, K. A. C. Elliott, E. Florey, *Nature* 178, 1052 (1956).
2. E. Florey, *Arch. intern. physiol.* 62, 33 (1954); E. Florey and H. McLennan, *J. Physiol.* 130, 446 (1955); K. A. C. Elliott and E. Florey, *J. Neurochem.* 1, 181 (1956).
3. C. Edwards and S. W. Kuffler, *Federation Proc.* 16, 145 (1957).
4. T. Hayashi and K. Nagai, *XX Intern. Physiol. Cong.* (1956), p. 410; T. Hayashi and R. Suhara, *ibid.* (1956), p. 410.
5. H. Grundfest, *Ann. N.Y. Acad. Sci.* 66, art.

3, 537 (1957) and *Physiol. Revs.*, in press (1957).
6. D. P. Purpura and H. Grundfest, *J. Neurophysiol.* 19, 573 (1956); and in press.
7. L. S. Goodman and A. Gilman, *The Pharmacological Basis of Therapeutics* (Macmillan, New York, 1955).
8. A. Geiger and S. Yamasaki, *J. Neurochem.* 1, 93 (1956).
9. T. Hayashi, *Chemical Physiology of Excitation in Muscle and Nerve* (Shoten, Tokyo, 1956).
10. We are indebted to Heinrich Waelsch, for a number of amino acids used in this work, and to G. F. Gestring, for technical assistance.
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25 February 1957

Serotonin and Histamine in Mast Cells

Previous investigations have demonstrated the presence of heparin (*1*) and histamine (*2*) in mast cells of various animal species. Asboe-Hansen (*3*) has presented evidence that these cells also produce hyaluronic acid. Recently, Benditt *et al.* (*4*) identified serotonin (5-hydroxytryptamine) in mast cell suspensions prepared from peritoneal washings of rats and found serotonin in rat skin in proportion to its mast cell content. Similar studies by Parratt and West (*5*) suggested that much of the serotonin, as well as histamine, in rat skin is held in the mast cells. The studies of Rowley and Benditt (*6*) in rats indicate that the edema-producing action of agents which damage mast cells may be mediated by "release" of both of these potent amines.

This is primarily a study of serotonin and histamine in mast cells of three animal species: mouse, dog, and man. Mice of the inbred strain DBA/2 and (BALB/c by DBA/2)F_1 hybrids bearing transplantable mast cell neoplasm P185 in subcutaneous solid tumor and ascitic forms (*7*) were made available for study during the 26th to 30th transfer generations. Several other reticular neoplasms in mice were obtained for assay. A first- and second-generation transplantable subcutaneous mast cell tumor of the dog was also used (*8*). Urine specimens were obtained from two patients with urticaria pigmentosa, a condition characterized histologically by dense accumulations of mast cells in the skin. In addition, a skin biopsy was obtained from one of these patients (*9*). Portions of skin from other patients were also studied.

The mouse tumor was composed chiefly of closely packed mast cells, whereas the dog tumor contained a considerable amount of fibrous tissue and a few eosinophils. Details of the discovery, technique of transplantation, and morphology of the mouse tumor have been presented by Dunn and Potter (*7*). One of the patients with urticaria pigmentosa also had skeletal involvement. A report of this case has been made by Zak, Covey, and Snodgrass (*10*). Chemical methods for the measurement of histamine, serotonin, and the serotonin metabolite, 5-hydroxyindoleacetic acid (5HIAA), were those developed previously in this laboratory (*11*).

The serotonin and histamine levels of various tissues are shown in Table 1. The solid mast cell tumors in mice contained large amounts of both serotonin and histamine, while in the dog tumor only the histamine concentration was elevated. Catechol amines could not be detected in the mouse tumor, and paper chromatographic studies showed serotonin to be the only 5-hydroxyindole present. Skin from the patient with urticaria pigmentosa contained a high level of histamine but insignificant amounts of serotonin. Measurements of urinary 5-hydroxyindoleacetic acid in the two patients with urticaria pigmentosa gave values of 5.1 to 7.2 mg/day (normal—2.0 to 9.0), confirming the finding that human mast cells do not contain serotonin.

It is known that carcinoid tumors, derived from the chromaffin cells of the intestinal tract, contain large amounts of serotonin and that patients with metastatic carcinoid excrete excessive amounts of 5-hydroxyindoleacetic acid in the urine (*12*). Recently, Waldenström *et al.* (*13*) reported an elevated urinary excretion of histamine in some of these patients and suggested the possibilities that some tumors might produce both serotonin and histamine or that the serotonin produced might liberate histamine from other tissues. Three carcinoid tumors were found to contain the usual large amount of serotonin but only a small amount of histamine (Table 1). If this is characteristic of all carcinoid tumors, then the increased histamine excretion by carcinoid patients must be a secondary phenomenon.

Table 1. Serotonin and histamine content of various tissues.

Material	Serotonin (μg/g)	Histamine (μg/g)
Tumors		
Mouse mast cell*	80–180	470–560
Dog mast cell	< 0.2	315, 160
3 human carcinoids	360, 570, 800	3.4, 2.0, 0.8
Other mouse tumors†	< 0.2	< 1
Human skin		
Urticaria pigmentosa	< 0.25	44
3 normals	< 0.7	4.7, 5.4, 5.0

* Several assays were done on pooled solid tumor specimens from a total of 20 DBA/2 mice.
† Several transplantable tumors (transfer generation indicated in parenthesis) were analyzed. In strain DBA/2: one type-A reticulum cell sarcoma, P228 (39) and one type-B, P195 (19), two lymphocytic, P228 (90) and P388 (63), and one granulocytic, P1081 (3); in strain C57BL: one lymphocytic, P1162 (5); in strain C3H: one well-differentiated plasma cell neoplasm, X5563 (8). A somewhat elevated amount of serotonin (22 μg/g) was found in a pooled sample of four poorly differentiated plasma cell neoplasms, 70429 (36) in strain C3H.

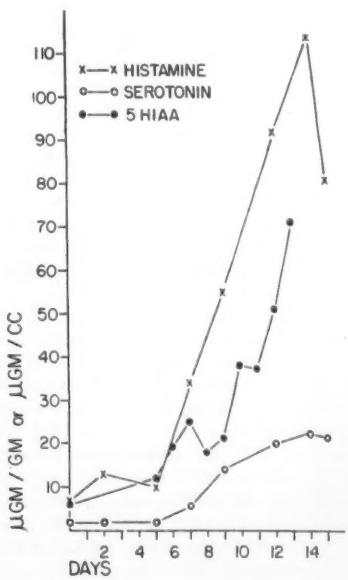

Fig. 1. Effect of mast cell tumor transplantation (ascitic form) on serotonin and histamine contents of whole mice (μg/g) and urinary excretion of 5-hydroxyindoleacetic acid (μg/ml). The animals usually died suddenly at 14 to 16 days.

The increased production of serotonin and histamine in tumor-bearing mice was studied in two ways. First, a group of 16 mice, (BALB/c by DBA/2)F_1, were placed in a metabolism cage after intraperitoneal injection of tumor cells, and urine was collected for assay for 5-hydroxyindoleacetic acid. Control values were obtained on a group of eight nontumor mice of the same strain, which were studied for 2 weeks. Second, serotonin and histamine assays were done on homogenates of pairs of whole mice at various intervals after tumor transplantation. The results, shown in Fig. 1, indicate that there was a marked production of both substances in association with growth of tumor. A simple test for excretion of excessive amounts of urinary 5-hydroxyindoles, useful in the clinical diagnosis of carcinoid (*14*), also became positive in the tumor-bearing mice.

Assuming that the abnormal mast cells in the three species studied produce serotonin or histamine, or both, in a manner comparable to that of normal mast cells, a marked species variation is clearly

shown. It is well to bear this in mind when one attempts to relate results of animal experimentation to human physiology. It will be of interest to compare the cellular catalysts of serotonin- and nonserotonin-containing mast cells (*15*).

A. SJOERDSMA
T. P. WAALKES
H. WEISSBACH

Clinic of General Medicine and Experimental Therapeutics and *Laboratory of Clinical Biochemistry, National Heart Institute, Bethesda, Maryland*

References and Notes

1. J. E. Jorpes, *Heparin in the Treatment of Thrombosis* (Oxford Univ. Press, London, ed. 2, 1946), p. 59; J. Oliver, F. Bloom, C. Mangieri, *J. Exptl. Med.* 86, 107 (1947).
2. J. F. Riley and G. B. West, *J. Physiol.* 120, 528 (1953).
3. G. Asboe-Hansen, *Ann. Rheumatic Diseases* 9, 149 (1950).
4. E. P. Benditt *et al.*, *Proc. Soc. Exptl. Biol. Med.* 90, 303 (1955).
5. J. R. Parratt and G. B. West, *J. Physiol.* 132, 40P (1956).
6. D. A. Rowley and E. P. Benditt, *J. Exptl. Med.* 103, 399 (1956).
7. T. B. Dunn and M. Potter, *J. Natl. Cancer Inst.*, 18, 587 (1957).
8. The cooperation of T. B. Dunn, M. Potter, and L. S. Lombard (National Cancer Institute) in supplying neoplastic material is gratefully acknowledged.
9. Skin biopsy and urine specimens on one patient were supplied by M. J. Davis and James C. Lawler, department of dermatology, Walter Reed Army Institute of Research, Washington, D.C.
10. F. G. Zak, J. A. Covey, J. J. Snodgrass, *New Engl. J. Med.* 256, 56 (1957).
11. T. P. Waalkes and H. Weissbach, *Proc. Soc. Exptl. Biol. Med.* 93, 394 (1956); S. Udenfriend, H. Weissbach, C. T. Clark, *J. Biol. Chem.* 215, 337 (1955); S. Udenfriend, H. Weissbach, E. Titus, *ibid.* 216, 499 (1955).
12. A. Sjoerdsma, H. Weissbach, S. Udenfriend, *Am. J. Med.* 20, 520 (1956).
13. J. Waldenström, B. Pernow, H. Silwer, *Acta Med. Scand.* 156, 73 (1956).
14. A. Sjoerdsma, H. Weissbach, S. Udenfriend, *J. Am. Med. Assoc.* 159, 397 (1955).
15. The technical assistance of Consuelo Garcia is acknowledged.

15 March 1957

Changes of Body Weight in Normal Men Who Stop Smoking Cigarettes

The role of overweight and obesity in the development of so-called degenerative diseases (*1*) and, consequently, the factors that affect body weight continue to be of interest.

We are all familiar with the occasional large gains in weight among men who stop smoking. Surprisingly enough, the phenomenon of weight change following a break in a lifelong pattern of smoking, which is not associated with intercurrent illness or a medically supervised dietary regimen designed to reduce or to increase body weight (*2*), has not been studied systematically. One reason for the absence of such information is the fact that longitudinal investigations on the "normal" adult man are difficult to carry out.

This study (*3*) was undertaken within the wider framework of researches on aging, focused on factors that are associated with the development of "degenerative" (noninfectious, noncongenital) heart disease and carried on in the Laboratory of Physiological Hygiene, University of Minnesota, since 1947. A group of approximately 300 business and professional men, examined at yearly intervals, serve as subjects. The laboratory staff refrains from giving advice to them, but findings indicative of the presence of disease are reported to their personal physicians. We wish to study the effects of the differences in the mode of life.

The "experimental" subjects are men who voluntarily stopped smoking cigarettes and on whom weight data are available for 2 years before and 2 years after the year in which they stopped smoking. A control group was obtained by selecting men who did not stop smoking and were matched in age, relative body weight (actual weight expressed as a percentage of "standard" weight for sex, age, and height), and actual body weight at the beginning of the first year of the 5-year period, without reference to weight trends during the rest of the period. The means and standard deviations and the t-tests of significance of the differences between means of the experimental and the control groups, respectively, were 49.8 ± 4.2 and 51.2 ± 3.5 years ($t = 1.20$, nonsignificant) for age; 97.5 ± 11.9 and 97.7 ± 11.2 ($t = 0.05$, nonsignificant) for relative body weight; and 75.8 ± 9.2 and 75.8 ± 9.2 kg for absolute body weight. Thus, at the outset, the two groups did not differ significantly in respect to any of the three criteria that were considered for matching. Both groups represent "normal," middle-aged men, with body weight close to their age standard. The intensity and total duraion of smoking were similar.

Longitudinal observations on smoking and body weight are summarized in Table 1. Using the average weights for years 1 and 2, and for years 4 and 5, we obtained, in the control group, a small (1.1 lb), statistically nonsignificant decrement while, in the experimental group, there was a substantial (8.2 lb), statistically highly significant rise. The respective t-values refer to t-tests for paired varieties; with $(N\text{-}1)$, that is, 20 degrees of freedom, the reference value $t_{0.001} = 3.850$. On comparing the mean difference between the change in the experimental and matched group, we obtain a net difference of 4.23 kg (9.3 lb), which is also statistically highly significant; in this case the t-tests were calculated for unpaired variates, with $2(N\text{-}1)$, that is, 40 degrees of freedom. The corresponding $t_{0.001} = 3.551$.

Table 1. Mean weights, weight changes, and differences in weight change between the two groups.

Item	Experimental group	Control group
Weight (kg) for years 1 plus 2	76.05	76.36
Weight (kg) for years 4 plus 5	79.78	75.86
Weight change		
Mean	+3.73	−0.50
Standard deviation	±1.94	±3.03
t within group	5.65*	1.18
Weight change difference (kg)	4.23	
Weight change difference, t between groups	5.39*	

* Statistically highly significant.

It should be emphasized that both our groups consisted of essentially "normal" men. We have not included several individuals who stopped smoking because of intercurrent coronary heart disease or in whom a rigorous dietary (reducing) regimen, together with termination of smoking on medical orders, was a part of therapy.

The present data provide information on interindividual variability in the weight gain, its average amount, and its statistical significance. The question of permanence of the gain beyond 2 years remains open. While the evidence concerning the effect on body weight of stopping cigarette smoking is convincing, no simple and definite interpretation of the phenomenon can be offered. Experimental observations on the inhibition of gastric hunger contractions by smoking (*4*) and the increase in tobacco consumption among individuals who are maintained on reduced calorie intake (*5*) suggest that smoking tends to depress the felt need for food.

J. BROŽEK
A. KEYS

Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, Minneapolis

References and Notes

1. J. Brožek and A. Keys, *Geriatrics* 12, 79 (1957).
2. A. E. Koehler, E. Hill, N. Marsh, *Gastroenterology* 8, 208 (1947).
3. This work was supported, in part, by grants provided by the Tobacco Industry Research Committee and the National Heart Institute, U.S. Public Health Service [grant H10 (C11)].
4. R. C. Batterman, in *The Biologic Effects of Tobacco*, E. L. Wynder, Ed. (Little, Brown, Boston, 1955), p. 140.
5. A. Keys *et al.*, *The Biology of Human Starvation* (Univ. of Minnesota Press, Minneapolis, 1950), p. 830.

27 March 1957

Book Reviews

Optics. Bruno Rossi. Addison-Wesley, Reading, Mass., 1957. 510 pp. Illus. $8.50.

This is a textbook for the advanced undergraduate student. A familiarity with the calculus is assumed, and some simple differential equations are developed and solved.

By basing the book on the wave model of light, Rossi has achieved a high degree of logical unity and consistency. Huygens' principle is discussed in unusually great detail in the first chapter, where it is shown that rectilinear propagation follows logically from a consideration of light waves as pulses of short duration. With this foundation, the subject of geometric optics is developed in the second chapter. The wave model is extended from pulses to sinusoidal waves in the third and fourth chapters, which deal with interference and diffraction. The transverse nature of the waves is introduced in the sixth chapter, to account for polarization and double refraction. In the seventh chapter, light waves are identified as electromagnetic waves, and Maxwell's theory is developed. The optical properties of matter are interpreted in the eighth chapter, by considering interactions between electromagnetic waves and atomic oscillators. This theory is entirely classical, with no discussion of the quantum-mechanical treatment and its results. The final chapter reveals the limitations of classical theory and illustrates the complementary character of waves and particles in the theory of light.

The strength of this book is its logical and rigorous development of the consequences of the classical wave model of light. A weakness, as a textbook, is its beginning with a chapter that will be difficult for the student. Another obvious weakness is that there is no recognition of quantum theory until the very end of the book.

The problems that are associated with each chapter are an important extension of the text material. They often disclose practical applications of the preceding theory; for example, low-reflectance films and interference filters are not discussed in the text but are assigned as problems. Such topics are often not listed in the index.

Some conspicuous omissions are Abbe's sine law, the theory of stops, aberrations of optical systems, a criticism of the Fresnel-Kirchhoff theory of diffraction, and radiation theory. On the other hand, noteworthy inclusions are Abbe's theory of image formation, the phase-contrast microscope, a very good treatment of mechanical waves, and a development of the electromagnetic field of a moving charge. Chapter 9, on light quanta, is excellent.

The many line drawings are well done, but the halftones are flat and muddy. There are very few errors. The book is a very well-written and scholarly work and is an important addition to optical literature.

JOSEPH VALASEK
University of Minnesota

Advances in Food Research. vol. VII. E. M. Mrak and G. F. Stewart, Eds. Academic Press, New York, 1957. 404 pp. Illus. $8.50.

Volume VII of *Advances in Food Research* contains seven articles, each concerned with a facet of research in food processing.

Three of the contributions deal with specific food products. Fish spoilage and preservation is discussed by Yukio Tomiyasu and Buhei Zenitani. The authors render a service in that much of the material reviewed in the section is Japanese and, according to the editors, has not been generally available outside of Japan. Under the title "Gelatin," Bernard Idson and Emory Braswell describe the technology of gelatin manufacture, the chemical and physical properties of gelatin and collagen, and some applications of gelatin in the food, pharmaceutical, and industrial fields. C. Nieman presents, in a similar article, the technology of licorice manufacture and the chemistry and pharmacology of licorice and some of its components.

Three of the articles are concerned with problems that are encountered in food processing and marketing in general. The discussion of "Water relations of food spoilage microorganisms," by W. J. Scott, reviews some basic physical and biological concepts of these relations, the information on water requirements for growth of the organisms, and applications of knowledge of the relations in food preservation. Walter A. Mercer and Ira I. Somers describe the use of chlorine in sanitation of food-processing plants. The history of the use of chlorine, the technology of application, and the effects of chlorine in plant sanitation are discussed. Jean F. Caul's article, "The profile method of flavor analysis," recounts the development of this method of analyzing and classifying flavor. The selection and training of panels and their procedure in developing "flavor profiles" are described.

The seventh article, "Freeze-drying of food products," by J. C. Harper and A. L. Tappel, describes in detail the status of development and the fundamentals of the freeze-drying process. The authors discuss methods and equipment used in freeze-drying as well as present and prospective applications of the process. The process is, essentially, still in the research stage of development. Areas in which additional research is needed are listed.

Each of the articles includes an extensive bibliography, and the volume contains author and subject indexes.

The purpose of a work of this kind is, of course, to bring together information for the use, primarily, of persons in the specified field of endeavor. If the information available is adequately reviewed and is set forth in usable form, as it seems to be in the present case, the objective of the volume has been attained. The reader, however, might wish for improvement in literary style in some of the articles in this volume. At the least, such improvement would add to the pleasure with which the material is read. In some cases, the ease and perhaps the accuracy with which the information is transmitted to the reader would be enhanced.

PAUL E. JOHNSON
Food Protection Committee, National Research Council

Science and Economic Development: New Patterns of Living. Richard L. Meirer. Technology Press, Cambridge; Wiley, New York; Chapman and Hall, London, 1956. 266 pp. $6.

Although the present world scene is overshadowed by political tensions and their economic and strategic concomitants, much greater concern should be felt about the ever-widening gap between the rapid progress of contemporary sci-

ence and the almost stationary status of social and educational institutions. This is especially true in the underdeveloped countries of the world, which will soon find themselves confronted with patterns of life to which they will be able to adjust only by a slow process of undisturbed development.

Most writers dealing with this grave problem of our time approach it from one of two diametrically opposite angles: they picture, in extravagant terms, the enormous possibilities which modern science and technology offer for the material benefit of mankind, with scant attention to man himself, or they envision economic and social utopias which are more the product of wishful thinking than of a realistic appraisal of technologic opportunities and social possibilities.

While both groups fail to give an integrated picture of the impact of modern science and technology on the social, psychological, and moral behavior of man as an individuum and a part of the community, R. L. Meirer draws from his large fund of knowledge in both the natural and the social sciences to give us a refreshing and provocative appraisal of the most probable course of events, considering both technologic and social factors. As a scholar trained in the exact sciences, he starts, naturally enough, with a sound attempt to quantify material human needs and world resources. He does not ignore spiritual requirements but does not complicate the picture by irrational and imponderable factors. Some agreement exists among scientists concerning an adequate level of living, and human needs can be expressed quantitatively in terms of nutrients, water, fiber, energy, and construction material. Estimates can be made of the availability of the world's renewable resources under conservative application of present agricultural, forestry, and fishery practices, and the probable reserves of nonrenewable resources will permit some extrapolations, provided that some minor resources such as uranium or titanium do not suddenly become major ones.

Where we reach the field of conjecture—namely, in the application of very recent discoveries in the physical and biological sciences to more efficient resource management—we find the book at its best, for it is always scientifically exact, technically sound, and directed toward a world as it is and not as it ought to be. Whether the author speaks about the protein problem, which he correctly considers the most fundamental in human nutrition, or of opportunities for expanding the protein supply by better utilization of marine resources, pisciculture in fresh waters, or growing of algae and other microorganisms, he always remains within the domain of proved scientific facts and technical experience. In one respect only could he have enlarged his exposition of maximal resource exploitation—that is, in the field of wild terrestrial vegetation, of which man uses only about 0.2 percent. There is no reason why the vast catabolism of organic matter, through bacterial and fungal decomposition (especially in the rain-soaked forests of the tropics and subtropics), could not be channeled toward an orderly degradation into useful products without impairing the cycle of nutrient metabolism in nature.

In the chapter on new fuels, the author deals lucidly with the utilization of solar energy, biological photosynthesis, nonbiological photosynthesis, and water- and wind-power as well as with utilization of atomic energy. He estimates the fossil fuel supply at 3×10^{19} calories. The yield of other energy sources, especially that of the "big unknown," atomic energy, cannot even be conjectured. There is no question that energy requirements for food, transportation, thermal comfort, and industry, especially in some newer metal-reduction processes, will increase rapidly, but so also will man's efficiency in utilizing energy.

In the most fascinating chapter of the book, Meirer tries to appraise the impact of this enormous expansion of human knowledge and productive capacity on the structure of society and the patterns of living. True scientist that he is, he meets this difficult problem objectively, without political bias or preconceived opinions. He realizes that the economically underdeveloped countries are not only suffering from overpopulation, or rather underemployment, but are continuously caught in a vicious economic cycle. Because of the low income-level, the people have a tendency to consume all their earnings and are unable to save. This naturally inhibits formation of domestic capital. Since low income is largely due to shortage of capital, the economy remains depressed. This lack of capital is the main factor in the ever-widening gap between scientific discoveries and their application. Only by way of international cooperation between the capital-rich and the capital-poor nations can satisfactory development of the world be brought about, and eventual disaster averted. However, such cooperation should be administered so as to leave the greatest possible freedom of self-expression and development of spiritual values to less advanced peoples.

All in all, this is an excellent book, written by a man who, as a chemist and physicist (University of California) and as an economist (Manchester School of Economic and Social Studies), is on good speaking terms with both natural and social scientists. While the former have lately become concerned with the consequences of their scientific research and discoveries, the latter are paying more and more attention to the dynamics of social and economic developments (especially in the less developed areas of the world), brought about by the progress and the application of science and technology. To both, the book is highly recommended.

FRANCIS J. WEISS
U. S. Operations Mission to Nicaragua

The Organization of the Cerebral Cortex. D. A. Sholl. Methuen, London; Wiley, New York, 1956. 125 pp. Illus. $4.25.

The Organization of the Cerebral Cortex is a summary of some interesting anatomical studies on the cerebral cortex. The point of view is that of quantitative cytological neuroanatomy. D. A. Sholl has some interesting data, from extensive silver preparations, on the distribution and extent of dendritic branchings. He attempts to relate these data to a theory of cortical activity based on connectivity and critical thresholds for excitation.

This theory has succeeded in mimicking one kind of cortical activity—that is, the slow spread of certain spontaneous figures of electric activity under deep Nembutal anesthesia. Such kinds of cortical activity may be confined to states of anesthesia, sleep, toxicity, and epileptic seizures. However, it may be that such mechanisms exist, operate, and are masked in the case of unanesthetized cortex that is bombarded by nonsynchronized activities.

The illustrations are excellent, and the bibliography is useful.

JOHN C. LILLY
National Institute of Mental Health, National Institutes of Health

Structure Reports for 1940–1941. vol. 8. A. J. C. Wilson, Ed. Published for the International Union of Crystallography. Oosthoek, Utrecht, Netherlands, 1956. 383 pp. Fl. 80.

The publication of *Structure Reports for 1940–1941* completes the coverage of all essential molecular structure information for solids, liquids, and gases obtained during the period 1913–50 and published in *Structurbericht*, volumes 1–7 (1913–39), and *Structure Reports*, volumes 8–13 (1940–50). The data for 1952 are now being assembled, and those for 1951 are presumably in press. This

is work of inestimable value to crystallographers, mineralogists, metallurgists, chemists, solid-state physicists, and all who are concerned with studying the structure of matter. It is an ever-increasing, monumental task, and the editors and reporters are to be congratulated on having maintained, in this volume, the high standard of accurate and critical reporting that has come to be associated with *Structure Reports*.

In contemplating the series as it now stands, three questions come to mind. First, should an effort be made to increase the rate of production beyond one volume a year in order to bring the series up to date? Second, in view of the inevitable increase in size and cost of subsequent volumes, should the price be reduced to maintain a wide distribution and to enable private subscribers to continue their support? Third, is the time ripe to revise the rationalization of crystal structure types that was given in volumes 1, 2, and 3? In my opinion, the answer to all three questions is definitely in the affirmative. It is, however, a remarkable tribute to the original compilers that the descriptions of structure types in volumes 1 and 2 of *Strukturbericht* are still very useful and in so many respects have stood the test of time.

It may very well be that these objectives could be achieved only by means of a considerable financial subsidy. If this is so, I take this opportunity to urge the International Union of Crystallography to seek such funds as are necessary to project into the future this indispensable means of coping with the increasing multiplicity of scientific papers.

G. A. JEFFREY
University of Pittsburgh

Handbuch der Physik. vol. XXXIII, *Optics of Corpuscles.* S. Flügge, Ed. Springer, Berlin, 1956. 702 pp. DM. 122.50.

Optics of Corpuscles, volume XXXIII of the new edition of the famous *Handbuch der Physik,* originally edited by Geiger and Scheel, deals with subject matter which, in the original "blue" *Handbuch,* covered a small space and was treated in different sections. It deals with methods and instruments that are based on the action of electric and magnetic fields on moving, electrically charged particles. These fields, when properly shaped, have deviating and focusing effects on charged particles in motion, as have lenses, mirrors, and prisms on light rays. All instruments that are based on this action of electric and magnetic fields are treated in this volume, and this leads to an arrangement of articles which, at first glance, appears to be peculiar. However, under the aspect of electron and ion optics, they are tied together in a natural way.

The arrangement of the different chapters appears as an analog to that expected in a treatment of instruments in light optics, in which a natural sequence would be formed by the discussion of light sources, the general theory of image formation on the basis of geometric optics, followed by a digression into wave optics in connection with a discussion of resolving power of instruments in general. This would be followed by the treatment of optical instruments, including microscopes and spectroscopes. This logical sequence is followed, in the present volume, with articles on electron and ion sources, electron and ion optics, electron microscopes, mass spectroscopes, and finally beta-ray spectroscopes.

The first article, by Detlev Kamke (Germany), is restricted mainly to electron and ion sources which are of importance for the subsequent contributions of this volume. Ion sources used in accelerators are not included; discussion of these is reserved for volume XLIX. This article is of a technical nature, and nearly two-thirds of the space is used for description of the different electron and ion guns.

The contribution on electron and ion optics by W. Glaser (Austria), is written by a first-rate expert in this field. More than one-third of the whole volume is devoted to this fundamentally important topic. The presentation excels in clarity and conciseness. One of the eight chapters is devoted to a discussion of image formation on the basis of wave mechanics.

The article on electron microscopes, written by S. Leisegang (Germany), gives, in about 150 pages, a thorough and attractive treatment of the fundamental aspects, a clear presentation of the different commercially available instruments, and a discussion of theoretical and practical limitations of electron microscopy.

A vivid account of the historical development and of the present state of mass spectroscopy is presented by H. Ewald (Germany) in his contribution entitled "Mass spectroscopic apparatus." All important types are described, and the discussion of their performance is elucidated by excellent reproductions of mass spectrograms.

The final section, on beta-ray spectroscopes, is written by T. R. Gerholm (Sweden) and is the only article of the volume written in English. It deals mainly with the instrumentation for the study of nuclear disintegration and nuclear structure. (An extensive theoretical and experimental treatment of beta-ray spectroscopy is to be included in volumes XLI, XLII, and XLV of this encyclopedia.) After a brief historical survey, the fundamental principles are discussed, and a treatment of the different instruments is given. This contains also a critical comparison of the different types. Two subsequent chapters are devoted to high-precision beta- and gamma-ray spectroscopic technique as it is applied to gamma-ray spectroscopy. An appendix contains a six-figure table for conversion of $B\rho$-values (electron momentum values) into electron energies, and vice versa, and covers the range from 0.9 kev to about 30 Mev.

Each section of the volume closes with a bibliography, which, in general, covers the years up to 1954 and, in some cases, to 1955. These same years are covered by the numerous references given in the text.

Layout, printing, and especially the numerous illustrations are of excellent quality. The only weak point is the inadequacy of the subject index, which is given in German-English and English-German. An encyclopedia of this type is intended to serve not only as a source of detailed information but also as a book of reference, and for the latter purpose the index should comprise many more entries than those that are given in the present volume. It would be better to have one complete index in one language than two deficient ones in two languages.

K. W. MEISSNER
Purdue University

Heterocyclic Compounds. vol. 5, *Five-Membered Heterocycles Containing Two Hetero Atoms and Their Benzo Derivatives.* Robert C. Elderfield, Ed. Wiley, New York; Chapman and Hall, London, 1957. 744 pp. Illus. $20.

These treatises on heterocyclic compounds constitute a real service to organic chemists, biochemists, and pharmacologists, since the authors have brought together information that is spread through hundreds of journals and books. The mass of material has been so well organized that future investigators will be saved the time and labor of doing it individually.

There are eight chapters in volume 5: "1,3-Dioxolane and its derivatives" (44 pages), by R. C. Elderfield and F. W. Short (1,2-Dioxolanes, which are essentially cyclic peroxides, are omitted, and 1,4-dioxanes are treated in volume 6); "Pyrazoles and related compounds" (117 pages), by T. L. Jacobs; "Indazoles" (32 pages), by Elderfield; "Imidazoles and condensed imidazoles" (104 pages), by E. S. Schipper and A. R. Day; "Oxazole and its derivatives" (120

pages), by J. W. Cornforth; "Benzoxazoles and related systems" (34 pages), also by Cornforth; "Isoxazoles" (32 pages), by R. A. Barnes; and "Thiazoles and benzothiazoles" (239 pages), by J. M. Sprague and A. H. Land. The pages are an index of the extent of the research work that has been reported on each of these ring systems.

Each chapter has an individual table of contents. The nomenclature and numbering scheme for each heterocyclic system are given, followed by discussions of structure, tautomerism, and resonance. The important syntheses, reactions, and physical and pharmacological properties are then treated in a critical fashion.

The authors and editor have done an excellent job of covering the literature and of organizing the material. The book is well printed and remarkably free from errors. An expanded general index assists greatly in locating specific topics. The book can be recommended to all scientists who are in need of an up-to-date survey of these heterocyclic ring systems.

RALPH L. SHRINER
University of Iowa

New Books

Alcoholism. Basic aspects and treatment. A symposium held under the auspices of the American Association for the Advancement of Science in cooperation with the American Psychiatric Association and the American Physiological Society and presented at the Atlanta, Ga., meeting, 27–28 Dec. 1955. AAAS Publ. No. 47. Harold E. Himwich, Ed. American Association for the Advancement of Science, Washington, D.C., 1957. 212 pp. Members, $5; nonmembers, $5.75.

Selected Papers in Statistics and Probability by Abraham Wald. Edited for the Institute of Mathematical Statistics. T. W. Anderson, committee chairman. Stanford University Press, Stanford, Calif., 1957 (copyright 1955, McGraw-Hill, New York). 711 pp. $10.

Laboratory Glass-Working for Scientists. A. J. B. Robertson, D. J. Fabian, A. J. Crocker, and J. Dewing. Academic Press, New York; Butterworths, London, 1957. 198 pp. $4.

Botany. Carl L. Wilson and Walter E. Loomis. Dryden, New York, rev. ed., 1957. 528 pp. $7.25.

Genus Pentremites and Its Species. Geological Society of America memoir 69. J. J. Galloway and Harold V. Kaska. Geological Society of America, New York, 1957. 113 pp.

The Structure of Nucleic Acids and Their Role in Protein Synthesis. Biochemical Society symposium No. 14 held at the London School of Hygiene and Tropical Medicine, 18 Feb. 1956. E. M. Crook, Ed. Cambridge University Press, Cambridge, England, 1957 (order from Cambridge University Press, New York 22). 74 pp. $3.75.

Parthenogenesis and Polyploidy in Mammalian Development. R. A. Beatty. Cambridge University Press, Cambridge, England, 1957 (order from Cambridge University Press, New York 22). 143 pp. $3.

Russian-English Atomic Dictionary. Eugene A. Carpovich. Technical Dictionaries Co., Box 144, New York 31, N.Y. 317 pp. $12.

Voluntary Health Insurance in Two Cities. A survey of subscriber-households. Odin W. Anderson, research director, Health Information Foundation, and the staff of the National Opinion Research Center. Harvard University Press, Cambridge, Mass., 1957. 158 pp. $5.

Bioenergetics. Albert Szent-Györgyi. Academic Press, New York, 1957. 153 pp. $4.50.

Frequency Modulation Receivers. J. D. Jones. Philosophical Library, New York, 1957. 123 pp. $6.

V.H.F. Television Tuners. D. H. Fisher. Philosophical Library, New York, 1957. 143 pp. $6.

Energetics in Biochemical Reactions. Irving M. Klotz. Academic Press, New York, 1957. 71 pp. $3.

Zoology. Alfred M. Elliott. Appleton-Century-Crofts, New York, ed. 2, 1957. 746 pp. $7.

Biology. Claude A. Villee. Saunders, Philadelphia, 1957. 635 pp.

A Textbook of Histology. Alexander A. Maximow and William Bloom. Saunders, Philadelphia, ed. 7, 1957. 628 pp.

Exploring with Your Microscope. Julian D. Corrington. McGraw-Hill, New York, 1957. 235 pp. $4.95.

The Psychology of Careers. An introduction to vocational development. Donald E. Super. Harper, New York, 1957. 372 pp. $5.75.

Clinical Toxicology of Commercial Products. Acute poisoning (home and farm). Marion N. Gleason, Robert E. Gosselin, and Harold C. Hodge. Williams & Wilkins, Baltimore, Md., 1957. 1160 pp. $16.

Physical Science for Liberal Arts Students. Hugo N. Swenson and J. Edmund Woods. Wiley, New York; Chapman & Hall, London, 1957. 333 pp. $6.50.

Chromatography, a Review of Principles and Applications. Edgar Lederer and Michael Lederer. Elsevier, Amsterdam, ed. 2, 1957 (distributed by Van Nostrand, Princeton, N.J.). 731 pp. $12.75.

Technology and Social Change. Francis R. Allen, Hornell Hart, Delbert C. Miller, William F. Ogburn, and Meyer F. Nimkoff. Appleton-Century-Croft, New York, 1957. 529 pp. $7.

The Temple of Jerusalem. Studies in Biblical archaeology No. 5. Translated by B. E. Hooke. Andre Parrot. Philosophical Library, New York, 1955. 112 pp. $2.75.

Vector Analysis. Louis Brand. Wiley, New York; Chapman & Hall, London, 1957. 295 pp. $6.

Experimental Research on Ageing. Symposium of the Biological and Medical Research Committee of the International Gerontological Association's European Section. Basel, 4–7 Apr. 1956. F. Verzar, Ed. Birkhauser, Basel, 1956. 290 pp. F. 34.

Thermodynamics, an Advanced Treatment for Chemists and Physicists. E. A. Guggenheim. North-Holland, Amsterdam, ed. 3, 1957. 476 pp. $9.75.

Galactic Nebulae and Interstellar Matter. Jean Dufay. Translated by A. J. Pomerans. Philosophical Library, New York, 1957. 352 pp. $15.

Die Periphere Innervation. Emil Villiger. Benno Schawbe, Basel, 1957 (order from Intercontinental Medical Book Corp., New York 16). 210 pp. $5.

Cytology and Cytogenetics. Carl P. Swanson. Prentice-Hall, Englewood Cliffs, N.J., 1957. 596 pp. $13.35.

Insight, a Study of Human Understanding. Bernard J. F. Lonergan. Philosophical Library, New York, 1957. 815 pp. $10.

Science and Human Life. J. A. V. Butler. Basic Books, New York, 1957. 172 pp. $3.95.

Elastic Waves in Layered Media. Lamont Geological Observatory contribution No. 189. W. Maurice Ewing, Wenceslas S. Jardetzky, and Frank Press. McGraw-Hill, New York, 1957. 391 pp. $10.

Light, Vegetation and Chlorophyll. J. Terrien, G. Truffaut, and J. Carles. Translated by Madge E. Thompson. Philosophical Library, New York, 1957. 228 pp. $6.

BCG Vaccination against Tuberculosis. Sol. R. Rosenthal. With sections by Camille Guerin, Bernard Weill-Halle, and Arvid Wallgren. Little, Brown, Boston, 1957. 389 pp. $7.50.

Microbial Ecology. Seventh symposium of the Society for General Microbiology held at the Royal Institution, London, Apr. 1957. Cambridge University Press, Cambridge, England, 1957. 396 pp. $6.50.

Glacial and Pleistocene Geology. Richard F. Flint. Wiley, New York; Chapman & Hall, London, 1957. 566 pp. $12.50.

Essays in Metabolism. The John Punnett Peters number of the *Yale Journal of Biology and Medicine.* Louis G. Welt, Ed. Little, Brown, Boston, 1957. 207 pp. $6.50.

Bibliography of Parapsychology. Compiled by George Zorab. Parapsychology Foundation, New York, 1957. 127 pp.

Proceedings of Four Conferences of Parapsychological Studies. Parapsychology Foundation, New York, 1957. 180 pp.

Principles of Epidemiology. Ian Taylor and John Knowelden. Little, Brown, Boston, 1957. 307 pp. $9.

Ordovician Trilobites of Argentina. Special publ. 1, Department of Geology, University of Kansas. Horacio J. Harrington and Armando F. Leanza. University of Kansas Press, Lawrence, 1957. 276 pp. $6.

The Inheritance of Coat Color in Dogs. Clarence C. Little. Cornell University Press, Ithaca, N.Y., 1957. 194 pp. $4.

A Short Dictionary of Mathematics. C. H. McDowell. Philosophical Library, New York, 1957. 76 pp. $2.75.

Radiation: What It Is and How It Affects You. Jack Schubert and Ralph E. Lapp. Viking, New York, 1957. 314 pp. $3.95.

Clinical Pathology in General Practice. Specially commissioned articles from the *British Medical Journal.* Lippincott, Philadelphia, Pa., 1957 (published in Great Britain in 1955) 330 pp. $5.

Meetings and Societies

Observation and Interpretation

Do the processes of physical observation and measurement have absolute limits of some kind, or are these only an artifact of a particular interpretation of these processes? How serious are (or would be) such limits for the predicting and explanatory (interpretative) functions of science, supposing that probability statements are still available? The most interesting property of these questions is their capacity to evoke confident but incompatible answers from theoretical physicists. After more than 30 years we certainly should have some answers, and it is perhaps a little embarrassing that we cannot come near to agreeing on *the* answers. These questions are on the borderland of philosophy and physics and, like their ancestors which produced the theories of inertia and relativity, are the keys to many doors; but their answers are the keyholes. The 1957 symposium of the Colston Research Society [a group of Bristol (England) citizens who finance the venture] invited a number of the most capable physicists and philosophers in Europe to reexamine these issues, and an excellent program resulted. The symposium was held at the University of Bristol, 31 Mar.–5 Apr. The papers and the subsequent discussions will be published, and I shall therefore confine myself to listing them and giving some general comments, which must be understood as the personal impressions of one observer.

The main issue was the Bohr-Einstein dispute over the status of quantum mechanics, which is held by the former to be in some sense final and by the latter to be essentially an *incomplete* account of micro-processes. Among those who delivered papers, the Copenhagen school was represented particularly by Rosenfeld (Manchester) and Süssmann (Göttingen and Munich), a student of Heisenberg's. The Einstein position was developed by Bohm (Haifa) in his paper "A proposed explanation of quantum theory in terms of hidden variables at a subquantum-mechanical level" and was supported by Vigier (Institut Henri Poincaré, Paris). Among the other contributions that were in the category of theoretical physics, indirect support for the first position was provided by Groenewold (Groningen) ("Objective and subjective aspects of statistics in quantum description") and for the second, by Bopp (Munich). Fierz (Basel) ("Does a physical theory comprehend an 'objective, real, single, process'?") and Feyerabend (Bristol) ("On the quantum theory of measurement") had their sympathies with the former viewpoint, one inferred. The papers were commendably brief, and the discussion periods were considerably longer, with the result that the party lines were quite soon made clear and a vigorous dispute continued from one session to the next. Only on the last day was there a feeling that the possible variations were exhausted and that a period of reconsideration would be required to produce new arguments.

It is very interesting to notice the role of the philosophic slogans adopted by the two sides in directing their arguments and their search for physical explanations; the Copenhagen school proclaimed the irrelevance of intuitive models to quantum events, and the "hidden variablists" insisted on the existence of a definite state in a system, regardless of the presence or activity of an observer. The importance of the slogans is not their logical relationship, for they are compatible, but the way in which they were the theme and last resort of each disputant; clearly, it was the interpretations and not the observations which were in question. Körner (Bristol) ("On philosophic arguments in physics") brought out well the strength of this linkage between the hard-pressed theoretician and the philosopher. Polanyi (Manchester) ("Beauty, elegance, and reality in science") attempted to explicate some of the formal criteria which enter into the judgment of theories at this level of great generality, where they become almost philosophic. (One recalls again the debates on absolute space, phlogiston, atoms, the continual-creation cosmologies, and so forth). Other logical problems of the borderline were taken up by Gallie (Belfast) ("The limits of prediction"), by Kneale (Oxford) ("What can we see?"), and by Ryle (Oxford) ("Predicting and inferring").

The dependence of interpretations of quantum theory on a particular (usually unstated) philosophic analysis becomes especially clear in connection with the concept of probability, since, for example, the debate over "information-waves versus real waves" is, in great part, a debate about the nature of probability. On this topic Popper (London School of Economics), Ayer (University College, London), and Braithwaite (Cambridge), as logicians, produced three good papers, whose relationship to the quantum theory could well have been discussed at greater length.

The 25 symposiasts who did not read papers provided a critical and enlightened audience, whose selectivity avoided a good deal of the usual time-wasting that is associated with convention meetings on these topics. I found myself particularly interested in the comments, either on or off the floor, of Cohen (Dundee), Hesse (University College, London), Mackay (King's College, London), Müller (Braunschweig), and O'Connor (Liverpool). Of course, others would make other choices, but I doubt that there would be much dispute over the outstanding grasp of the field exhibited by Groenewold, whose introduction of the Einstein-Podolski-Rosen paradox as a difficulty for Bohm's interpretation and whose analysis of the von Neumann proof were very impressive. Although he argues that the von Neumann proof tells us nothing about the possibility of subquantum theories which include the quantum laws as derivations, he also thinks that any such theory is *very likely* to collapse over one or more of a range of special difficulties—a view which he supported by a verbal analysis of the mathematics of the three best contemporary candidates.

It remains to be seen, of course, whether Bohm can derive the Dirac equations and the other well-established formulas and then whether some differentiating experiments support his position. One interesting result of the discussion was a design for such a differentiating experiment, which was accepted by both sides. But Groenewold's objections would still make it impossible to regard the theory as deterministic in the usual sense, which in this case constitutes a serious conceptual difficulty.

It remains only for me to say that the symposium was organized with great courtesy and efficiency by Korner, assisted by Pryce, Edgeley, and Feyerabend, of the host university; that the hospitality provided by the Colston Society and the university was very generous and cordial; and that all who listened learned.

MICHAEL SCRIVEN
Department of Philosophy, Swarthmore College, Swarthmore, Pennsylvania, and *Minnesota Center for Philosophy of Science*

American Institute of Physics

The American Institute of Physics (AIP), founded in 1931, is a federation of the major societies of physics in the United States. The member societies are the American Physical Society, the Optical Society of America, the Acoustical Society of America, the American Association of Physics Teachers, and the Society of Rheology. The combined membership of these societies, together with some associate members of the institute, now totals more than 18,000 individuals. All of these societies are affiliated with the AAAS, and the American Institute of Physics has recently become an affiliate.

The institute is governed by a board whose members are nominated by the member societies, except for three who are elected by popular ballot of the individual members. The board appoints an executive committee, and the institute has a director and an executive secretary, with a supporting professional staff. The AIP was the first of a number of similar federations in various fields of science and served in some respects as a model for the others. The member societies are fully autonomous. They control their own terms of membership, elect their own officers, arrange their own scientific meetings, and edit their own journals. The societies delegate to the institute the mechanics of all their publishing work as well as various developmental and representative functions which can best be accomplished on behalf of physics as a whole by combining the strength of the societies through the institute.

The major activity of the institute is publication of the following journals: for the American Physical Society, *Physical Review, Reviews of Modern Physics,* and *Bulletin of the American Physical Society*; for the Optical Society, *Journal of the Optical Society of America*; for the Acoustical Society, *Journal of the Acoustical Society of America* and *Noise Control*; for the American Association of Physics Teachers, *American Journal of Physics*; under AIP sponsorship, *Review of Scientific Instruments, Journal of Chemical Physics, Journal of Applied Physics,* and *Physics Today.*

To this list of journals, the institute has recently added four periodical translations of journals that are published in Russian by the Academy of Sciences of the U.S.S.R. These journals, all subsidized by the National Science Foundation, are *Soviet Physics–J.E.T.P., Soviet Physics–Technical Physics, Soviet Physics–Doklady,* and *Soviet Physics–Acoustics.*

By arrangement with the member societies, the institute supplies secretarial, clerical, and fiscal services, as desired, to the secretaries, treasurers, and other officers of the societies, and frequently assists the societies in some aspects of the business of arranging their meetings.

Among the general services that are rendered by the AIP to physics and to the general community are the distribution of vocational information about physics, the sponsoring of student sections at universities and colleges, the maintenance of the physics section of the National Register of Scientific and Specialized Personnel, sponsored by the National Science Foundation, and cooperation with societies and institutes in other fields of science in such joint enterprises as the Scientific Manpower Commission. The institute also operates a number of projects on grants from the Government or from private foundations; all of these are designed to develop the science of physics, to improve education in the science, or to attract suitable students to careers in physics.

The work of the institute has grown to such magnitude—involving the publication of 19,000 pages per year, service to its 18,000 members, and the carrying on of various assigned projects—that it has become necessary to move to larger quarters. A drive for a "development fund" of $500,000 is now in progress. Half of this is for the conversion of a building, which has been purchased, into enlarged office space for the institute's work. The remainder is for a needed expansion of publishing services and for other activities designed to strengthen the profession of physics in the United States. Early in June, the institute will move from its present quarters to the new location at 335 E. 45 St., New York.

HENRY A. BARTON
American Institute of Physics, New York, New York

Society Elections

■ Association of Vitamin Chemists: pres., Orton F. Hixson, Laboratory of Vitamin Technology; v. pres., Claire E. Graham, The Wilson Laboratories; treas., Buford H. Barrows, Hales and Hunter Co.; sec., Arnold E. Denton, Research Laboratories, Swift and Co., Chicago 9, Ill. Representative to the AAAS Council is Henry C. Spruth.

■ South Dakota Academy of Science: pres., John Willard, South Dakota School of Mines and Technology; 1st v. pres., S. W. Howell, Yankton College; 2nd v. pres., V. R. Nelson, Augustana College; sec.-treas., John M. Winter, Dept. of Botany, State University of South Dakota, Vermillion. The representative to the AAAS Council is Raymond Greb, South Dakota State College.

■ Population Association of America: pres., Harold F. Dorn, National Institute of Health, Bethesda, Md.; pres. elect, Dorothy Swaine Thomas, University of Pennsylvania; 1st v. pres., Kingsley Davis, University of California, Berkeley; 2nd v. pres., Dudley Kirk, Population Council, Inc., Scarsdale, N.Y.; sec.-treas., Daniel O. Price, University of North Carolina, Chapel Hill.

■ American Association of Colleges of Pharmacy: pres., Tom D. Rowe, University of Michigan, Ann Arbor; v. pres., J. F. McCloskey, Loyola University, New Orleans, La.; exec. comm. chairman, Louis C. Zopf, State University of Iowa, Iowa City; sec.-treas., George L. Webster, University of Illinois, Chicago 12.

■ Virginia Academy of Science: pres., William G. Guy, College of William and Mary; pres. elect, John C. Forbes, Medical College of Virginia; sec., Paul M. Patterson, Hollins College, Hollins, Va.; treas. and representative to the AAAS Council, Foley F. Smith, Virginia Alcoholic Beverage Control Board; asst. sec.-treas., William B. Wartman, Jr., American Tobacco Company Research Laboratory.

Forthcoming Events

July

10–17. **International Union of Crystallography, 4th genl. assembly, Montreal, Canada. (G. A. Jeffrey, Chemistry Dept., Univ. of Pittsburgh, Pittsburgh 13, Pa.)**

11–13. **Applied Cytology, European Symp., Brussels, Belgium. (Secretary, Comm. on International Cong., American Cancer Soc., 521 W. 57 St., New York 19, N.Y.)**

14–19. **International Assoc. of Gerontology, Merano, Italy. (A. I. Lansing, Dept. of Anatomy, Univ. of Pittsburgh, Pittsburgh 13, Pa.)**

14–20. **Clinical Pathology, 4th internatl. cong., Brussels, Belgium. (M. Welsch, Service de Bacteriologie et de Parasitologie, Université de Liége, Blvd. de la Constitution, Liége, Belgium.)**

15–18. **Biochemistry of Lipids, International Colloquium, Oxford, England. (Dr. Sinclair, Laboratory of Human Nutrition, Oxford.)**

15–19. **Institute on College Administration, annual, Ann Arbor, Mich. (A. D. Henderson, 2442 U.E.S., Univ. of Michigan, Ann Arbor.)**

16–19. **American Malacological Union, annual, New Haven, Conn. (Miss M. C. Teskey, P.O. Box 238, Marinette, Wis.)**

16–24. **International Cong. for Pure and Applied Chemistry, 16th, Paris, France (R. Morf, Secy. Genl., IUPAC, Sandoz, S.A., Basel, Switzerland.)**

20–21. **Medical-Sociological Aspects of Senile Nervous Diseases, internatl. symp., Venice, Italy. (S. N. Feingold, Jewish**

Vocational Service of Greater Boston, 70 Franklin St., Boston 10, Mass.)

21–28. Neurological Sciences, 1st internatl. cong., Brussels, Belgium. (P. Bailey, National Institutes of Health, Bethesda 14, Md.)

23–24. Modern Electrochemical Methods of Analysis, Internatl. symp., Paris, France. (G. Charles, Ecole Superieure de Physique et de Chimie, 10, rue Vauquelin, Paris 5e.)

25–26. Structure Properties Relationships of Polymers (IUPAC), Paris, France. (International Union of Pure and Applied Chemistry, 4, Avenue de l'Observatoire, Paris 6e.)

25–29. Protein Chemistry Symp., IUPAC, Paris, France. (J. Roche, College de France, Place Marcellin Berthelot, Paris 5e.)

26–27. Experimental Psychology and Animal Behavior Section of International Union of Biology, Brussels, Belgium. (H. S. Langfeld, Dept. of Psychology, Princeton Univ., Princeton, N.J.)

26–27. Linguistic Soc. of America, Ann Arbor, Mich. (A. A. Hill, Box 7790, University Station, Austin 12, Tex.)

26–27. Military Psychology, internatl. symp., Brussels, Belgium. (National Academy of Sciences, 2101 Constitution Ave., NW, Washington 25.)

26–31. International Humanist and Ethical Union, 2nd cong., London, England. (American Humanist Assoc., Gate House, Yellow Springs, Ohio.)

26–1. International Congress on Nutrition, 4th, Paris, France. (Quatrième Congrès International de Nutrition, CNERNA, 71, boulevard Péreire, Paris 17e.)

27–3. Religion in the Age of Science, 4th annual, Star Island, Isles of Shoals, Portsmouth, N.H. (Mrs. R. Holt, Box 156, Pennington, N.J.)

28–1. Psychoanalysis, 20th internatl. cong., Paris, France. (Dr. Nacht, 187, rue Saint-Jacques, Paris 5.)

28–3. Psychology, 15th internatl. cong., Brussels, Belgium. (L. Delys, 296, avenue des Sept Bonniers, Forest-Bruxelles.)

31–5. International Assoc. for Hydraulic Research, Lisbon, Portugal. (M. Coelho Mendes da Rocha, Laboratorio Nacional de Engenharia Civil, Avenida do Brasil, Lisbon.)

31–6. Dermatology, 11th internatl. cong., Stockholm, Sweden. (C. H. Floden, Hudkliniken, Karolinska Sjukhuset, Stockholm 60.)

August

2–3. Pennsylvania Acad. of Science, Honesdale, Pa. (K. Dearolf, Public Museum and Art Gallery, Reading, Pa.)

5–11. Pan American Cong. of Pediatrics, 5th, Lima, Peru. (C. F. Krumdieck, Washington 914, Lima.)

5–17. Curare and Curare-Like Agents, internatl. symp., Rio de Janeiro, Brazil. (C. Chagas, Instituto de Biofisica, Universidade do Brasil, 458 Avenida Pasteur, Rio de Janeiro.)

6–9. Poultry Science Assoc., annual, Columbia, Mo. (C. B. Ryan, Texas A.&M. College, College Station.)

7–9. Industrial Applications of X-Ray Analysis, 6th annual conf., Denver, Colo. (J. P. Blackledge, Metallurgy Div., Denver Research Inst., Univ. of Denver, Denver 10.)

7–9. International Union against the Venereal Diseases and the Treponematoses, 31st general assembly, Stockholm, Sweden. (Secretary General, Institut Alfred Fournier, 25, boulevard Saint-Jacques, Paris 14e, France.)

8–15. International Statistical Inst., 30th, Stockholm, Sweden. (Secretary General, ISI 30th Session, Fack, Stockholm 5.)

8–15. International Union for the Scientific Study of Population, Stockholm, Sweden. (F. Lorimer, c/o American University, Washington 16.)

11–14. Heat Transfer, national conf., University Park, Pa. (G. M. Dusinberre, Pennsylvania State Univ., University Park.)

11–17. World Federation for Mental Health, 10th annual, Copenhagen, Denmark. (Miss E. M. Thornton, 19 Manchester St., London, W.1, England.)

12–16. Canadian Teachers' Federation, annual, Edmonton, Alberta, Canada. (G. G. Croskery, 444 MacLaren St., Ottawa 4, Ont.)

12–18. Theory of Functions, internatl. colloquium, Helsinki, Finland. (B. Eck-

mann, Ecole Polytechnique, Federale, Zurich, Switzerland.)

12–25. International Soc. of Soil Mechanics and Foundation Engineering, 4th Conf., London, England. (A. Banister, Institution of Civil Engineers, Great George St., London, S.W.1.)

18–21. American Astronomical Soc., Urbana, Ill. (J. A. Hynek, Smithsonian Astrophysical Observatory, 60 Garden St., Cambridge 38, Mass.)

19–21. National Council of Teachers of Mathematics, Northfield, Minn. (M. H. Ahrendt, NCTM, 1201 16 St., NW, Washington 6.)

19–22. American Veterinary Medical Assoc., annual, Cleveland, Ohio. (J. G. Hardenbergh, AVMA, 600 S. Michigan Ave., Chicago 5, Ill.)

19–23. Clay Conf., 6th natl., Berkeley, Calif. (Dept. of Conferences and Special Activities, Univ. of California Extension, Berkeley 4.)

19–23. Clinical Chemistry, 2nd international European cong., Stockholm, Sweden. (K. Agner, Box 12024, Stockholm 12.)

19–24. Finite Groups, internatl. colloquium, Tübingen, Germany. (H. Wielandt, Faculty of Mathematics and Natural Science, Eberhard-Karls-Universität, Tübingen.)

(See issue of 17 May for comprehensive list)

LETTERS

The editors take no responsibility for the content of the letters published in this section. Anonymous letters will not be considered. Letters intended for publication should be typewritten double-spaced and submitted in duplicate. A letter writer should indicate clearly whether or not his letter is submitted for publication. For additional information, see Science **124**, *249 (1956) and* **125**, *16 (4 Jan. 1957).*

Literature, Science, Manpower Crisis

Unusual importance attaches to the article on "Literature, science, and the manpower crisis" by Joseph Gallant [*Science* **125**, 787 (26 Apr. 1957)]. If it could be read by all those who are engaged in building high school curriculums, by a large proportion of those who teach in upper primary and secondary schools, by those who write textbooks for these grades, by those who train teachers, and by key members of state and city boards of education, the shortage of scientists and technologists would surely soon be reduced; and, even more far-reaching and contrary to present reasonable expectation, a start might soon be made toward making basic scientific concepts acceptable in American culture. During the 50 years that I have been a reader of *Science* I have found neither in its pages nor elsewhere an equally cogent statement of the prime sources of present educational deficiency or failure in the sciences.

Two sentences will recall the core of the contribution: The problem centers in the high school. Involved there is practically the whole of the curriculum —not merely science and mathematics, but literature, history, and other of the humanities as well. Fortune has left it for a scholar in literature, and one actively teaching in a famous New York high school, to *document* satisfactorily the definite (and ultimately persuasive) prescientific bent of humanistic teaching in our high schools and, to point sharply to the resulting dichotomy in the basic thought and motivation of our people, involving an over-all denigration of the status and concepts of science. I quote: "But the humanities sweepingly ignore the role played by scientific insight and thinking in the ideology of our times and disdainfully march on their archaic way as though the atomic and electronic age had not arrived. . . . students must be attracted to the study of sciences, not *after* they are enrolled in the colleges, but *before*; not after they have elected physics and chemistry in the secondary schools, but before they do so. Moreover . . . they must be endowed with a perspective that will provide them with a profound and continuing motivation to apply themselves."

A clear, persuasive, and unhedged statement illuminating this much-

avoided center of our prime cultural problem has now appeared in *Science*. This statement supplies conclusive evidence that our "manpower crisis" is an inseparable part of the more inclusive cultural problem and, apart from the latter, will not be solved adequately by the various helpful measures already envisaged or employed. Presumably, the potential of this exceptional publication is convertible to the actual only through making the article available to many or all of the hundreds of thousands mentioned here. Even such wide distribution of a powerful challenge would doubtless early meet only partial success; but a worse outcome awaits a neglect of this supplement to current "manpower" efforts, and surely much fresh interest in the manpower problem should now favor some success to a definitely directed urge that scientific concepts become respectable in our secondary education. Thus we arrive at questions of practical action: Can *Science,* or can individual or collective scientists, devise or provide means to that end? Where republication? Costs of lists, and of mailing reprints? In the annals of research these items seem something less than gigantic or formidable, but perhaps they can and will block a promissing perceptible lift to both national safety and culture.

OSCAR RIDDLE

Plant City, Florida

Joseph Gallant's major thesis that all insights into the nature of the universe are the proper province of literature [*Science* **125**, 787 (1957)] appears well-taken. It is rather to support his contention than to cavil at it that one may question the correctness of his assertion that there are almost no contemporary instances of poetic integration of scientific concepts beyond the three cases he cites (Robinson Jeffers, Archibald MacLeish, and Mark Van Doren). Perhaps too much reliance was placed on the showing of exhaustive research in Helen Plotz' *Imagination's Other Place,* since from merely casual recollection it is possible to cite among the notable omissions from this anthology such names as those of Max Eastman, James Franklin Lewis, Alfred Noyes, Selden Rodman, A. M. Sullivan, and William Carlos Williams. Perhaps the list would grow more readily if the editorial board of *The Scientific Monthly* would reinstate F. L. Campbell's policy of publishing such work.

WILLIAM NEWBERRY

Olin Mathieson Chemical Corporation, New Haven, Connecticut

"I own the soft impeachment" of William Newberry's letter. If I have overlooked particular poems which utilize scientific concepts, it is because these poems are not among the best known works of the poets cited nor those that

are regarded by critics as representative of the poet's work—with the possible exception of the work of William Carlos Williams, for the omission of which there can be no excuse.

But this oversight on my part only highlights the more the fact that the scientific orientation of a poet's thoughts or emotions is the one aspect that literary discussion and criticism consistently neglect. This in turn emphasizes the urgency of focusing attention on the relationship of science to poetry and to literature in general.

On the curricular and pedagogic level the implication for me is that some agency should be set up to cull our imaginative literature, both prose and poetry, for revealing instances of the successful integration of scientific ideas and images with lyrical or imaginative expression and to bring these to the attention of teachers and students through recommended reading lists and anthologies. These will, in time, affect the standard syllabi and the standard literary anthologies. Such an agency would have to be charged with both research and public education.

On the creative and critical levels, new works incorporating the scientific outlook might be fostered by conferring the recognition and prestige of scientific bodies on them in some way, or by setting up an agency to do so, which might be a link between the humanities and science.

It might be well for scientific societies, the various manpower agencies, or associations of technologic firms to consider creating such an agency for its ultimate effect on our culture and our scientific manpower resources. What seems to be most needed is an instrument for closer liaison of the humanities and science, not only in organizational terms (between, say, scientific professional groups and literary and scholarly associations), but also in terms of research, intercommunication, and publicity.

JOSEPH GALLANT
Theodore Roosevelt High School,
New York, N. Y.

Radiation and Health

I can only partially agree with the statements expressed in your editorial, "Radiation and health" [*Science* **125**, 719 (19 Apr. 1957)]. The information on the radiation genetics of our species is exceedingly meagre, and currently we are forced to extrapolate from data collected by radiation geneticists working on the mouse, fruitfly, and various plants and microorganisms. To collect data for our species, we shall have to gather every scrap of information that results from each sizable exposure of the human reproductive system to ionizing radiation. Presumably, such exposures can occur accidentally or from medical diagnostic and therapeutic procedures.

I will grant that a record of exposures may be of no value to the individual keeping it, since the decision to expose this individual to further x-rays is primarily governed by the need for medical diagnosis or therapy. This is not the point, however. The value of records of this kind is that as they accumulate and the pedigrees of exposed individuals become available, only then can the geneticist attempt, from an analysis of these data, to determine the exact magnitude of the radiation hazard to the human germ plasm.

When one is ignorant admit it, proceed cautiously, and attempt to remedy the situation. In genetics, as G. Mendel has observed, the only way to remedy ignorance is to engage in the bookkeeping necessary for the construction of pedigrees. The answer to the question "Would the considerable effort required to keep such records for a large part of the population be worth while?" is an unqualified *Yes.*

ROBERT C. KING
Department of Biological Sciences,
Northwestern University,
Evanston, Illinois

EQUIPMENT NEWS

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Science *does not assume responsibility for the accuracy of the information. All inquiries concerning items listed should be addressed to* Science, *Room 740, 11 W. 42 St., New York 36, N.Y. Include the name(s) of the manufacturer(s) and the department number(s).*

■ FLUORITE VACUUM SPECTROMETER, manufactured by Hilger and Watts, Ld., permits use of emission lines in the far-ultraviolet for analysis of carbon, phosphorus, and sulfur in steels. The optical system of the instrument is housed in a drumlike container 18 in. in diameter. The four detectors, one for each element and one for the internal standard, are quartz-window multiplier phototubes. Samples are mounted in a chamber through which inert gas is circulated. The time required for analysis is less than 3 min. (Jarrell-Ash Co., Dept. S383)

■ PULSE-HEIGHT ANALYZER sorts electric pulses arriving at random time intervals into 100 channels, according to their amplitude. The analyzer converts pulse height to time, sorts the resulting time measurements, and stores the count in each channel in quartz delay-line storage elements. The accumulated distribution of pulses is displayed on a cathode-ray tube. (Nucleonic Corporation of America, Dept. S375)

■ SAMPLE FEED DEVICE for electrochromatography consists of a slow-speed motor, a syringe clamp and syringe, and an actuating cam. Motor speed is variable from 1 rev/min to 1 rev/7 days, thus providing, in combination with variations in the cam and in syringe size, a wide range of sample sizes and delivery rates. Dual or multiple units are available. (Microchemical Specialties Co., Dept. S370)

■ POWER TRANSIENT ANALYZER simultaneously measures, displays, and records generator output voltage, frequency, waveform, and power. Voltage and frequency errors are less than 0.1 percent. Recording and waveform display are accomplished with a string-galvanometer oscillograph. (American Machine and Foundry Co., Dept. S367)

■ TEMPERATURE PROBES use thermistors to sense temperature. Maximum operating temperature is 500°F. Time constants are 0.5, 4.0, and 7 sec for available models. Nominal resistance may be 1000 ohm to 0.5 Mohm or more. All structural parts are of stainless steel. (Rosemount Engineering Co., Dept. S368)

■ ULTRASONIC CLEANER is used for cleaning bearings and delicate mechanisms. Transducers are barium titanate operating at a frequency of 35 to 40 kcy/sec. Output is 150 w. Tanks are stainless steel. (Labline Inc., Dept. S348)

■ LIQUID LEVEL SENSER operates on the principle that the terminal impedance of an ultrasonic transducer depends strongly on whether it is air loaded or liquid loaded. The senser is capable of detecting liquid level to an accuracy of ± 1/32 in. Foam or clinging droplets do not affect its performance, nor do the characteristics of the liquid affect the change of impedance. Operating range is from −270° to +220°F. (Acoustica Associates Inc., Dept. S373)

■ INTERFERENCE MICROSCOPE is a surface-finish tester for highly polished surfaces with roughness heights of approximately 1 μ or less. It is designed for convex spherical and cylindrical surfaces. Operation is based on multiple-beam interferometry. The field of view is approximately 1.5 mm in diameter. Cylindrical surfaces from 10 to 100 mm in diameter are accommodated. The instrument is portable, operating on batteries or from electric outlets. (Ercona Corp., Dept. S372)

■ COUNTER of plug-in design uses a pair of magnetic cores as the counting element. Counting speed is 50 kcy/sec. Scales of 9, 10, and 11 are available. Outputs provide 40 v at high impedance and 4 v at low impedance. Operation requires a power supply of 150 v at 15 ma and 6.3 v at 0.3 amp. No visual readout is provided. (Magnetics Research Co., Dept. S381)

■ MANOMETER is read by a servomechanism in which a differential transformer is continuously positioned to be electrically centered about a float containing magnetic material. A proportional shaft position in the servo transmission is then analogous to the position of the liquid column. Sensitivities in excess of 1 μ have been achieved. Five standard ranges are available from 32 to 120 in. (Exactel Instrument Co., Dept. S376)

■ AIR SAMPLER filters air at rates of 18, 36, or 70 ft^3/min, depending on the filter paper used. Particles as small as 0.01 μ in diameter are said to be accurately sampled. Air flow is measured by a variable-orifice meter. The sampler is designed for 24-hour operation. (Staplex Co., Dept. S377)

JOSHUA STERN
National Bureau of Standards

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(a) Executive Director, State Association for Mental Health; graduate training in mental health field (for example, social work, sociology, psychology), preferably doctoral level; although may be substituted for formal training; $6500–$9000. **(b) Physiologist** well trained in mammalian physiology, **Biochemist** experienced in metabolism, and **Bacteriologist** experienced in immunology and tuberculosis studies to serve as research associates, medical school research department; $6500–$7500; Midwest. **(c) Chemist,** M.S. or Ph.D.; research department, 200-bed hospital; Ohio; $6000–$7000. **(d) Analytical Chemist,** Ph.D., to direct group of analytical chemists; new research center, large industrial company; Pacific Coast. **(e) Bacteriologist,** Ph.D., to direct manufacturing laboratories; various research programs; $5500–$8000; near Chicago. S6-2 Medical Bureau, Burneice Larson, Director, 900 North Michigan Avenue, Chicago. X

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Inquiries are to be addressed to Dr. T. E. Warren, Director, Saskatchewan Research Council, University of Saskatchewan, Saskatoon, Saskatchewan. 6/14, 21

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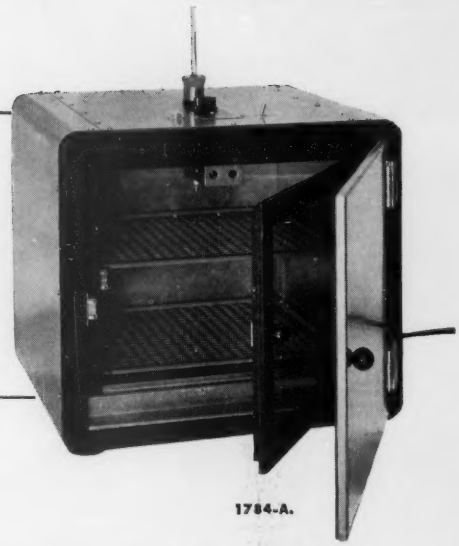

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